A

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

The Commissioner of Patents & Trademarks
Washington, D.C. 20231
Attn: Box Patent Application

Docket No. **PET 1638 D1**
Prior Application: PET 1638
Examiner: S. KUMAR
Art Unit: 1621

Sir: This is a request for filing a
☐ Continuation
☒ Divisional
Under 37 C.F.R. 1.53(b), of prior application Serial No. **09/039,266** filed on **March 16, 1998** of **Raphael Duval et al.**, for **Polymerized and Cross-Linked Chiral Compounds and Methods of Making Thereof**

1. ☒ Enclosed are **46** pages of the specification including claims and **0** sheets of drawings.
2. ☒ Enclosed is a copy of the oath or declaration as originally filed in Serial No. **09/039,266** on **March 16, 1998** in accordance with 37 C.F.R. §1.63(d).
3. ☒ The filing fee is calculated below:

FOR	NUMBER FILED	NUMBER EXTRA	RATE	FEE
TOTAL CLAIMS	48 - 20	28	$18	504.00
INDEPENDENT CLAIMS	7 - 3	4	$78	312.00
☐ MULTIPLE DEPENDENT CLAIM PRESENTED				
☐ Small Entity Status Claimed under 37 CFR 1.9 and 1.27		BASIC FEE		690.00
Statement(s): ☐ Attached ☐ Filed in Parent		TOTAL FILING FEE		$1506.00

jc586 U.S. PTO 09/541690 04/03/00

JC713 U.S. PTO 04/03/00

4. ☒ The amount of $ **1506.00** is included in the attached check.
   ☒ If a check is not attached, authorization is given to charge the amount indicated in the above sentence to Deposit Account No. 13-3402; two copies of this page being attached for this purpose.
5. ☐ Please charge my Deposit Account No. 13-3402 in the amount of $_____, two copies of this sheet are attached.
6. ☒ The Commissioner is hereby authorized to charge any deficiencies or credit any overpayment in payment of the following fees associated with this communication or otherwise due during the pendency of this application to Deposit Account No. 13-3402.
   ☒ Any filing fees under 37 CFR §1.16 for the presentation of extra claims.
   ☒ Any patent application processing fees under 37 CFR §1.17.
7. ☒ Cancel in this application original claims **11-17** of the prior application before calculating the filing fee.
8. ☒ Amend the specification by inserting before the first line the sentence:
   -- This is a ☐ continuation, ☒ divisional, of application Serial No. **09/039,266** filed **March 16, 1998**. --.
9. ☒ Priority of application No. **97/03,076** filed on **March 14, 1997** in **FRANCE** is claimed under 35 U.S.C. §119.
10. ☐ The certified copies have been filed in prior application Serial No. ___/_____ filed _____.
11. ☒ The prior application is assigned of record to **Institut Francais du Petrole and CHIRALSEP** both of **France**.
12. ☒ The power of attorney in the prior application is to: I. William Millen (19,544); John L. White (17,746); Anthony J. Zelano (27,969); Alan E.J. Branigan (20,565); John R. Moses (24,983); Harry B Shubin (32,004); Brion P. Heaney (32,542); Richard J. Traverso (30,595); Richard E. Kurtz (33,936); John A. Sopp (33,103); John H. Thomas (33,460); Richard M. Lebovitz (37,067) Luan C. Do (38,434) and Diana Hamlet-King (33,302)
    ☒ a. The power appears in the original papers in the prior application.
    ☒ b. Address all future communications to MILLEN, WHITE, ZELANO & BRANIGAN, P.C.
13. ☒ A preliminary amendment is enclosed.
14. ☐ Request for Transfer of Sequence Listing.
15. ☒ Incorporation By Reference.
    The entire disclosure of the prior application, from which a copy of the oath or declaration is supplied under Box 2, is considered as being part of the disclosure of the accompanying application and is hereby incorporated by reference therein.

Date: April 3, 2000

I. William Millen (Registration No. 19,344) - Attorney of Record
MILLEN, WHITE, ZELANO & BRANIGAN, P.C.
Arlington Courthouse Plaza I
2200 Clarendon Boulevard, Suite 1400
Arlington, Virginia 22201
(703) 243-6333

K:\PAT\PET\1638 D1\div trans form.wpd

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	:	**BOX PATENT APPLICATION**
Raphael DUVAL et al.	:	Examiner: S. Kumar
Serial No.: NEW	:	Group Art Unit: 1621
Filed: April 3, 2000	:	

For: POLYMERIZED AND CROSS-LINKED CHIRAL COMPOUNDS AND METHODS OF MAKING THEREOF

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Prior to examination, Applicants wish to amend the above-identified application as indicated below.

IN THE TITLE

Please amend the title as follows:

Please delete the title in its entirety and insert therefor

--Polymerized And Cross-Linked Chiral Compounds And Methods Of Making Thereof--.

IN THE SPECIFICATION

Please amend the specification as follows:

Page 1, before line 1, insert

--Field of the Invention--.

Page 1, before line 12, insert

--Background of the Invention--.

Page 5, before line 1, insert

--Summary of the Invention--.

Page 7, before line 8, insert

--Methods of the Invention--.

Page 12, before line 1, insert

--Polymerised and Cross Linked Chiral Compounds--.

Page 18, before line 5, insert

--Process for Synthesizing Polymers--.

Page 19, before line 1, insert

--Bifunctional Compounds--.

Page 20, before line 9, insert

--Chiral Compounds--.

Page 21, before line 15, insert

--Chiral Supports--.

IN THE CLAIMS

Please cancel claims 11-17 without prejudice or disclaimer.

Please amend the claims as follows:

Claim 3, line 1 (Amended):	Delete "or claim 2".
Claim 4, line 1 (Amended):	Replace "any one of claims 1 to 3" with --claim 1--.
Claim 5, line 1 (Amended):	Replace "any one of claims 1 to 3" with --claim 1--.

Claim 6,	**line 1 (Amended):**	Delete "or claim 5".
Claim 7,	**line 1 (Amended):**	Replace "any one of claims 1 to 3" with --claim 1--.
Claim 8,	**line 1 (Amended):**	Replace "any one of claims 4, 5 or 7" with --claim 4--.
Claim 18,	**line 1 (Amended):** **line 2:**	Replace "any one of" with --claim 13--; and delete "claims 13 to 17".
Claim 19,	**line 1 (Amended):** **Line 2:**	Replace "any one of" with --claim 13--; and delete "claims 13 to 17".
Claim 21,	**line 1 (Amended):** **line 2:**	Delete "any one"; and replace "of claims 13 to 19" with --claim 13--.
Claim 22,	**line 1 (Amended):** **Line 2:**	Replace "any one" with --claim 13--; and delete "of claims 13 to 20".
Claim 23,	**line 1 (Amended):** **line 2:**	Replace "to any" with --claim 13--; and delete "one of claims 13 to 20".
Claim 25,	**line 1 (Amended):**	Replace "any one of claims 21 to 24" with --claim 21--.
Claim 26,	**line 1 (Amended):** **line 2:**	Replace "any one" with --claim 13--; and delete "of claims 13 to 20".
Claim 27,	**line 1 (Amended):** **line 2:**	Replace "any" with --claim 13.--; and delete entirely.

Claim 28, line 2 (Amended): Replace "any one of claims 21to 27" with --claim 21--.

Please add the following new claims:

-- 29. A method comprising the following successive steps:

1) providing at least one bifunctional alkenyloxyaryl or alkenylaryloxyaryl compound of the formula $[R\text{-}CH{=}CH\text{-}(X)\text{-}O]_n\text{-}Ar\text{-}Q$, where Q is a group which reacts with a hydrogen carried by a heteroatom selected from the group consisting of oxygen, nitrogen and sulphur or a precursor thereof, and where:

n is in the range 1 to 20;

R is hydrogen or a linear of branched alkyl group or a linear or branched alkoxy group or a hydroxyl or an optionally substituted aryl group,

X is a divalent linear alkyl group containing more than one carbon atom, or a branched divalent alkyl group, or an aryl group optionally substituted with at least one group selected from the group consisting of hydrogen, alkyl, alkoxy, hydroxyl and trihalogenoalkyl;

Ar is an aryl or polyaryl group, optionally substituted with at least one hydrogen atom or at least one group selected from the group consisting of alkyl, alkoxy, hydroxyl, trihalogenoalkyl, silyl, thiol, amino, aminoalkyl, amide, nitro, nitrosamino, N-amino, aldehyde, acid, and ester; and

2) reacting at least one chiral compound containing at least one hydrogen of an alcohol, amine or thiol function with at least one group Q of the bifunctional compound of step 1), to synthesize at least one chiral compound.

30. A process according to claim 24, wherein said bifunctional compound is other than 4-allyloxyaniline, 4-allyoxybenzoic acid, an acid chloride of 4-allyoxybenzoic acid, and 4-allyoxyphenylisocyanate.

31. A process according to claim 10, wherein said bifunctional compound is other than 4-allyloxyaniline, 4-allyoxybenzoic acid, an acid chloride of 4-allyoxybenzoic acid, and 4-allyoxyphenylisocyanate.

32. A method comprising the following successive steps:

1) providing at least one bifunctional alkenyloxyaryl or alkenylaryloxyaryl compound with general formula $[R\text{-}CH{=}CH\text{-}(X)\text{-}O]_n\text{-}Ar\text{-}Q$,

where Q is -N=C=O or a precursor thereof; $-NH_2$ or $-CON_3$; -COCl or its precursor; -COOH; -N=C=S; or $-CH_2Y$, where Y is Cl or Br or I or methylsulphonyloxy or para-toluenesulphonyloxy or 3,5-dimethylphenylsulphonyloxy and where:

- n is in the range 1 to 20;
- R is hydrogen or a linear or branched alkyl group or a linear or branched alkoxy group or hydroxyl or an aryl group, optionally substituted;
- X is a linear alkyl group carrying more than one carbon atom or a branched alkyl group, or an aryl group, optionally substituted with at least one group selected from the group consisting of hydrogen, alkyl, alkoxy, hydroxyl and trihalogenoalkyl groups; and
- Ar is an aryl or polyaryl group, optionally substituted with at least one hydrogen atom or with at least one group selected from the group consisting of alkyl, alkoxy, hydroxyl, trihalogenoalkyl, silyl, thiol, amino, aminoalkyl, amide, nitro, nitrosamino, N-amino, aldehyde, acid and ester groups,
- excluding the following compounds: 4-allyloxyaniline, 4-allyloxybenzoic acid, its acid chloride, and 4-allyloxyphenylisocyanate

2) reacting at least one chiral unit containing at least one hydrogen of an alcohol, amine or thiol function with at least one group Q of the bifunctional compound of step 1), to synthesise at least one chiral compound.

33. A process for synthesising polymers comprising the following successive steps:

1) providing at least one bifunctional alkenyloxyaryl or alkenylaryloxyaryl type compound with general formula $[R\text{-}CH{=}CH\text{-}(X)\text{-}O]_n\text{-}Ar\text{-}Q$,

where Q is -N=C=O or a precursor thereof; $-NH_2$ or $-CON_3$; -COCl or its precursor; -COOH; -N=C=S; or $-CH_2Y$, where Y is Cl or Br or I or methylsulphonyloxy or para-toluenesulphonyloxy or 3,5-dimethylphenylsulphonyloxy and where:

- n is in the range 1 to 20;
- R is hydrogen or a linear or branched alkyl group or a linear or branched alkoxy group or hydroxyl or an aryl group, optionally substituted;
- X is a linear alkyl group carrying more than one carbon atom or a branched alkyl group, or an aryl group, optionally substituted with at least one group selected from the group consisting of hydrogen, alkyl, alkoxy, hydroxyl and trihalogenoalkyl groups; and
- Ar is an aryl or polyaryl group, optionally substituted with at least one hydrogen atom or with at least one group selected from the group consisting of alkyl, alkoxy, hydroxyl, trihalogenoalkyl, silyl, thiol, amino, aminoalkyl, amide, nitro, nitrosamino, N-amino, aldehyde, acid and ester groups,
- excluding the following compounds: 4-allyloxyaniline, 4-allyloxybenzoic acid, its acid chloride, and 4-allyloxyphenylisocyanate

2) conducting polymerization by the alkenyl moiety or by the R group of the bifunctional compound of step 1), to synthesize at least one polymer functionalized by a group Q.

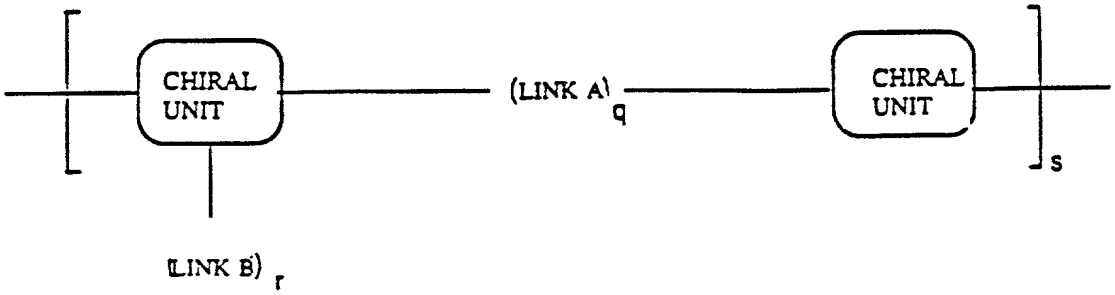
34. A process comprising polymerizing and cross-linking a chiral compound by reacting at least one hydrogen of an alcohol, amine or thiol function of at least one chiral unit of a product with at least one group Q of the bifunctional compound with the general formula $[R\text{-}CH{=}CH\text{-}(X)\text{-}O]_n\text{-}Ar\text{-}Q$,

where Q is a group which is reactive towards a hydrogen carried by a heteroatom selected from the group of oxygen, nitrogen or sulphur, or a precursor of such a group, and where:

- n is in the range 1 to 20;

- R is hydrogen or a linear or branched alkyl group or a linear or branched alkoxy group or hydroxyl or an aryl group, optionally substituted;
- X is a linear alkyl group carrying more than one carbon atom or a branched alkyl group, or an aryl group, optionally substituted with at least one group selected from the group of hydrogen, alkyl, alkoxy, hydroxyl or trihalogenoalkyl groups; and
- Ar is an aryl or polyaryl group, optionally substituted with at least one hydrogen atom or with at least one group selected from the group of alkyl, alkoxy, hydroxyl, trihalogenoalkyl, silyl, thiol, amino, amino, aminoalkyl, amide, nitro, nitrosamino, N-amino, aldehyde acid or ester groups

excluding the following compounds: 4-allyloxyaniline, 4-allyloxybenzoic acid, its acid chloride, and 4-allyloxyphenylisocyanate or its ester, amide, urea, carbamate, thioester or thiocarbamate derivatives with general formula (I):

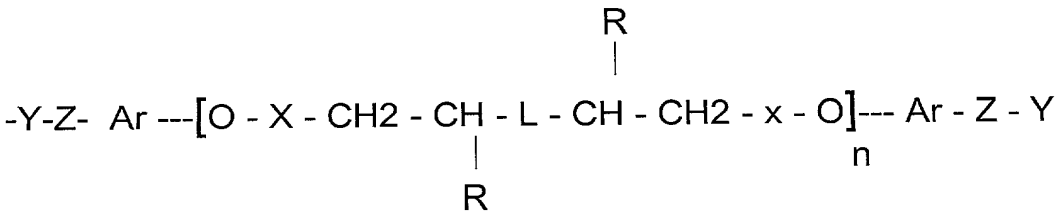


where:

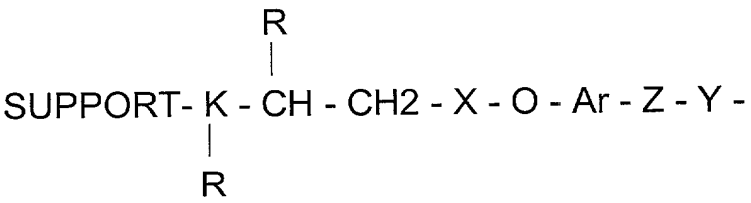
- q is at least 1 and less than 20;
- s is at least 1 and less than 20000;
- if r = 0, the compound is a pure cross-linked chiral polymer, oligomer or monomer;
- if r ≥ 1, the compound is a chiral polymer, oligomer or monomer which is cross-linked in a three-dimensional network andbonded to a cross-linked support;

LINK A represents:

R



Link B represents:



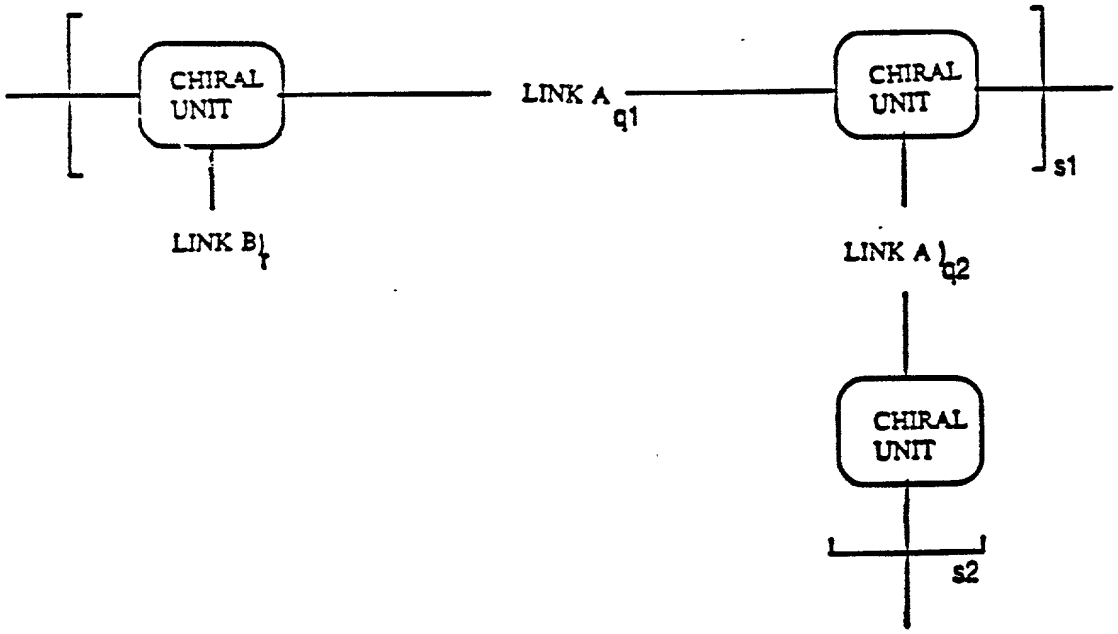
- "chiral unit" represents a monomeric, oligomeric, cyclooligomeric or polymeric chiral compound and optionally comprises a primary or secondary amine function or a primary, secondary or tertiary hydroxyl function or a sulphhydryl function and in which all or a portion of these functions have optionally been modified to the ester, amide, urea, carbamate, thioester or thiocarbamate;
- Z represents a $-CH_2-$ group or a -CO- group or a -NH-CO- group or a -NH-CS- group;
- Y represents a sulphur or oxygen atom or the amino group;
- n is in the range 1 to 20;
- Ar represents an aryl or polyaryl group
- X represents an alkyl or aryl group;
- R represents an alkyl group or hydrogen;
- L represents a single bond or a bis-sulphhydrayl or a silane or an ethylene group which may be substituted or a disiloxane;
- K represents a single bond or a siloxane or a silane;
- "support" represents an organic or mineral support; functionalized by an alkene or a hydrogenosilane or a sulphhydryl.

35. A process for polymerizing and cross-linking a chiral compound by reacting at least one hydrogen of an alcohol, amine or thiol function of at least one chiral unit of a product with at least one group Q of the bifunctional compound with the general formula $[R-CH=CH-(X)-O]_n-Ar-Q$,

where Q is a group which is reactive towards a hydrogen carried by a heteroatom selected from the group of oxygen, nitrogen or sulphur, or a precursor of such a group, and where

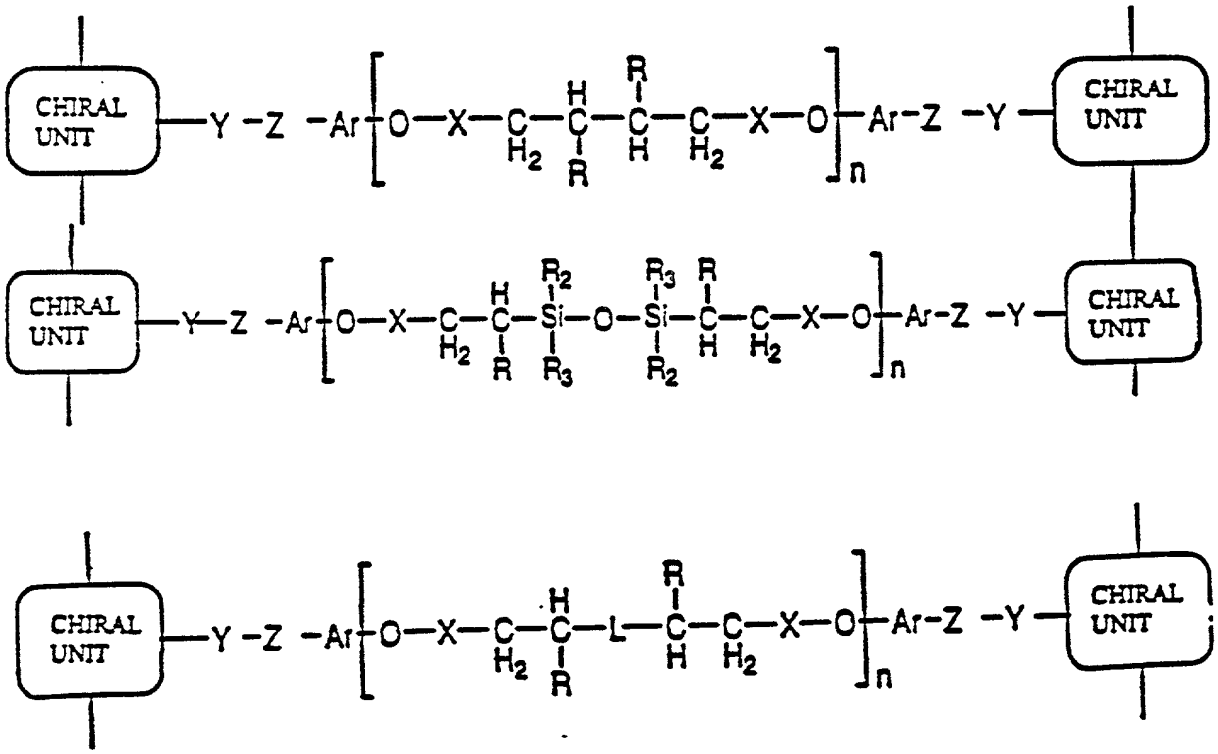
- n is in the range 1 to 20;
- R is hydrogen or a linear or branched alkyl group or a linear or branched alkoxy group or hydroxyl or an aryl group, optionally substituted;
- X is a linear alkyl group carrying more than one carbon atom or a branched alkyl group, or an aryl group, optionally substituted with at least one group selected from the group of hydrogen, alkyl, alkoxy, hydroxyl or trihalogenoalkyl groups; and
- Ar is an aryl or polyaryl group, optionally substituted with at least one hydrogen atom or with at least one group selected from the group of alkyl, alkoxy, hydroxyl, trihalogenoalkyl, silyl, thiol, amino, amino, aminoalkyl, amide, nitro, nitrosamino, N-amino, aldehyde acid or ester groups

excluding the following compounds: 4-allyloxyaniline, 4-allyloxybenzoic acid, its acid chloride, and 4-allyloxyphenylisocyanate or its ester, amide, urea, carbamate, thioester or thiocarbamate derivatives, with general formula:



- n is in the range 1 to 20;
- Ar represents an aryl or polyaryl group
- X represents an alkyl or aryl group;
- R represents an alkyl group or hydrogen;
- L represents a single bond or a bis-sulphhydrayl or a silane or an ethylene group which may be substituted or a disiloxane;
- K represents a single bond or a siloxane or a silane; and
- "support" represents an organic or mineral support; functionalized by an alkene or a hydrogenosilane or a sulphhydryl.

36. A process according to claim 18 wherein said polymerized and cross-linked chiral compounds has the following formulae:



37. A method according to claim 32, wherein the bifunctional compound is parapent-4-enoxybenoic acid.

38. A process according to claim 33, wherein the bifunctional compound is parapent-4-enoxybenoic acid.

39. A process according to claim 34, wherein the bifunctional compound is parapent-4-enoxybenoic acid.

40. A process according to claim 35, wherein the bifunctional compound is parapent-4-enoxybenoic acid.

41. A process according to claim 36, wherein the bifunctional compound is parapent-4-enoxybenoic acid.

42. A method according to claim 1, wherein the bifunctional compound is parapent-4-enoxybenoic acid.

43. A method according to claim 3, wherein the bifunctional compound is parapent-4-enoxybenoic acid.

44. A method according to claim 5, wherein the bifunctional compound is parapent-4-enoxybenoic acid.

45. A chiral compound according to claim 18, wherein the bifunctional compound is parapent-4-enoxybenoic acid.

46. A chiral compound according to claim 19, wherein the bifunctional compound is parapent-4-enoxybenoic acid.

47. A chiral support used to claim 21, wherein the bifunctional compound is parapent-4-enoxybenoic acid.

48. A process according to claim 28, wherein the bifunctional compound is parapent-4-enoxybenoic acid.--

REMARKS

The principle purpose of this Preliminary Amendment is to eliminate multiply dependent claims and the fee associated therewith, as well as adding new claims. Applicants reserve the right to reintroduce claims to canceled combined subject matter.

Respectfully submitted,

James E. Ruland (Reg. No. 37,432)
Attorney for Applicant(s)

MILLEN, WHITE, ZELANO & BRANIGAN, P.C.
Arlington Courthouse Plaza I
2200 Clarendon Blvd., Suite 1400
Arlington, VA 22201
Direct Dial: (703) 812-5338

Filed: March 30, 2000

IWM/JER/wks
K:\PAT\PET\1638 D1\preliminary amendment.wpd

The invention relates to a method which comprises synthesising bifunctional compounds then chiral compounds from the bifunctional compounds, also to synthesising supports comprising these chiral compounds, normally in the form of a cross-linked three-dimensional chiral network and generally with a modifiable degree of cross-linking depending on the desired degree of swelling, and the use of these supports for preparing and separating enantiomers, or for asymmetric synthesis. The invention also relates to bifunctional compounds, their use as a source of functionalised polymers, and to the chiral compounds, also to the use of these chiral compounds in a chiral support for separating and preparing enantiomers, principally for analytical or preparative chromatography, and for asymmetric synthesis.

Enantiomer separation is a field which has been expanding for about twenty years both on the preparative and on the analytical levels. This is particularly true in the pharmaceutical field, where the law requires the separate study of optical isomers of any chiral component of a medication composition. Substituted polysaccharides have been the subject of a number of studies, and celuloses physically deposited on a silica gel support are commercially available. Such compounds have the disadvantage, however, of usually being soluble in polar organic solvents, which drastically limits their applications.

Recent solutions to the problem of solubility have been found by forming covalent bonds between the substituted polysaccharide and the support. Kimata et al. have published their results ("Analytical methods and instrumentation", vol. 1, 23-29 (1993)) on a stationary chiral phase based on -tris-2,3,6(4-vinylbenzoate) cellulose deposited on silica gel, then polymerised on the support.

Chromatographic data obtained with two racemic test mixtures were as follows:

	Deposited support		Deposited and polymerised support	
	Stilbene oxide	1-(1-naphthyl ethanol)	Stilbene oxide	1-(1-naphthyl ethanol)
k'1	1.08	2.15	1.04	1.47
k'2	1.66	2.84	1.44	1.80
α	1.54	1.32	1.39	1.22
R_S	3.63	2.34	3.82	1.44

where:

- k'1 and k'2 are partition ratios, i.e., if i = 1 or 2, $k'_i = \frac{t_{R_i} - t_0}{t_0}$

where t_{R_i} is the retention time of compound i;

and t_0 is the non-retained solute transit time;

- α is the relative retention ratio: $\alpha = \frac{t_{R2} - t_0}{t_{R1} - t_0} = \frac{k'2}{k'1}$
- R_S is the peak resolution: $R_S = \frac{1}{4}\left(\frac{\alpha-1}{\alpha}\right)\left(\frac{k'2}{1+k'2}\right)(N)^{1/2}$

where N is the plate number

$$N = a\left(\frac{t_R}{\omega}\right)^2$$

where ω is the peak width at a given ordinate, related to the square of the standard deviation or variance σ^2 by the relationship $\omega^2 = a\sigma^2$, giving

$$N = 16\left(\frac{t_R}{\omega}\right)^2 = 5.54\left(\frac{t_R}{\sigma}\right)^2$$

A systematic reduction in the relative retention ratios obtained can be seen between the deposited support and the deposited and polymerised support: 10% less on the trans-stilbene oxide (α varies between 1.54 and 1.39) and 25% less for the 1-(1-naphthyl)ethanol.

This phenomenon can be explained by partial solubility of the polymerised support due to incomplete polymerisation because of weak reactivity of the vinyl benzoate group under the reaction conditions used.

Kimata et al. did not describe any examples of separation in a pure polar solvent.

Okamoto et al. (in European patent EP-B-0 155 637) described polymers which are chemically bonded to a silica gel. In particular, they described grafting tris-2,3,6-phenylcarbamate cellulose onto silica gel via a tritylated intermediate, then forming a covalent bond between the silica gel and the partially derived polysaccharide carbamate, by the action of a diisocyanate.

The results of elemental analyses carried out during the different stages of synthesis were as follows (EP-B-0 155 637, page 8 to page 9, line 33).

	C %	H %	N %
1. Trityl cellulose deposited on silica	15.40	1.23	0.09
2. Detritylated cellulose deposited on silica	3.61	0.60	-
3. Cellulose bonded to silica by toluene-2,4-diisocyanate	-	-	-
4. Cellulose phenyl carbamate bonded to silica and washed with THF/chloroform	3.23	0.27	0.45

The drop in the degree of grafting between the cellulose deposited on silica (2) and cellulose phenylcarbamate bonded to silica (4) is important knowing that the degree of (4) calculated after (2) is of the order of 14% of carbon. The loss of hydrocarbon moieties can thus be estimated to be 80% from formation of the covalent bond between the cellulose and the silica by the diisocyanate arm, followed by derivative formation by reacting the OH groups with phenyl isocyanate and final washing with chloroform.

No example of separation in polar solvents was given for the support obtained.

Okamoto et al (Japanese patent JP 06-206-893) have described an oligosaccharide chemically bonded to silica gel by means of an imine function reduced to an amine. Amylose is then chemicoenzymatically regenerated from this oligosaccharide. The available hydroxyl functions are then reacted with

carbamate functions to form derivatives. No example of separation in a polar solvent was given.

It is important to use a large column excess for preparative applications. The possibility of using 100% of chiral material in the form of pure polymer beads of substituted polysaccharides instead of physically depositing them on a support has proved effective in increasing mass yields in preparative chiral chromatographic processes. Thus patents EP-B-0 348 352, EP-B-0 316 270 and International patent application WO 96/27639 relate to the production of cellulose beads for separating optical isomers.

However, pure polymer beads are soluble in polar solvents such as halogenated solvents - tetrahydrofuran, dioxane, etc.. It is thus impossible to use these solvents either pure or in mixtures with high proportions of these solvents, to carry out isomer separation.

In order to overcome this disadvantage, Francotte et al. recommended irradiation polymerisation of polysaccharide derivatives. (WO 96/27615).

However, the degree of polymerisation appears to be difficult to control in such a process. No example of separation in a pure polar solvent is given.

Minguillon et al. described the synthesis of cellulose carbamates with partial derivatives formed by reaction with an undecenoyl chloride. However, the structure of the support was not explained (J. of Chromatog. A 728 (1996), 407-414 and 415-422).

Lange (US-A-5 274 167) described the polymerisation of optically active methacrylic acid derivatives, but the structure of the support was not explained. No example of separation in a pure polar solvent was given.

The present invention concerns the preparation of novel chiral compounds and their use in preparing or separating enantiomers, in particular on a support or in polymer beads.

The chiral supports are obtained in the form of pure polymer beads of the chiral compound which is normally polymerised and cross-linked, preferably into a three-dimensional glycosidic network or obtained in the form of a chiral compound attached to a support via a covalent bond, then polymerised and cross-linked, preferably into a three-dimensional glycosidic network.

The chiral supports of the invention have remarkable stability in polar solvents such as THF (tetrahydrofuran), chloroform, methylene chloride, acetonitrile, toluene, acetone or ethyl acetate.

For the first time, separation of a racemic molecule on a support based on a polysaccharide has been carried out in pure chloroform (see Examples IA, IB, IC and ID).

This exceptional stability towards polar solvents of the novel chiral supports is associated with the extremely fast mass transfer kinetics between the solutes and the three-dimensional glycosidic network. Again for the first time, separations have been carried out in the normal or inverse mode using an elution gradient on stationary chiral phases (see Examples IIA and IIB).

Further, we have noticed that the degree of cross-linking of the chiral supports has an influence on the swelling capacity of the supports. Since the swelling capacity is variable, there are difficulties in using it for analytical or preparative purposes in chromatographic processes: variable support volume, and the creation of large pressure drops during swelling can result in columns which are of insufficient size exploding or percolation becoming impossible for those which resist high pressures; also, during shrinking, dead volumes are seen to form which are incompatible with their current use.

The possibility of modifying the number and nature of the bifunctional compounds ensuring polymerisation and cross-linking per chiral unit has the advantage of enabling the degree of cross-linking and thus the final performance

of the chiral support to be modified and in particular the swelling capacity in polar solvents can be controlled.

Further, we have noticed that the use of polar solvents mixed with other alkane/alcohol type solvents can in some cases reverse the elution order of enantiomers of compounds of biological importance (see Example III). When analysing the enantiomeric purity of chiral molecules, the gain in sensitivity is thus significant. The compound which is eluted first is always that with a higher number of theoretical plates than the second.

For the same reasons, the first enantiomer eluted in a preparative chiral chromatographic process is always the most pure and the most concentrated. There is thus a major interest in analytical and preparative chiral chromatography is being able to control the order of enantiomer exit.

The three-dimensional glycosidic network of novel chiral supports thus offers this possibility through "matrix" effects, swelling to a greater or lesser extent depending on the degree of cross-linking of the support and the nature of the polar solvent used. Depending on the spatial disposition of the same functional constituents of each enantiomer, the matrix favours elution of one or other of the enantiomers by means of a variable three-dimensional structure.

The bifunctionality can bond chiral units, preferably glycosidic, via one or more covalent bonds to constitute a polymerised and cross-linked three-dimensional network and thus the degree of cross-linking depends on:

- the number of -OH, $-NH_2$, -NHR or SH functions in the chiral unit which have reacted or react with compounds:

  $[R\text{-}CH{=}CH\text{-}X\text{-}O]_nAr\text{-}Q$

  $[(R_1, R_2, R_3)Si\text{-}CH(R)\text{-}CH_2\text{-}X\text{-}O]_nAr\text{-}Q$

- the number n of these same formulae

where R, X, n, Ar, R_1, R_2, and R_3 are defined below.

The -OH, $-NH_2$ or SH functions are generally and preferably partially reacted to form derivatives in the case where polar solvents are to be used and to benefit from the "matrix" effects relating thereto. The degree of cross-linking of the network, preferably a three-dimensional chiral glycosidic network, is maximal and the swelling effects are also maximised; the use of gradient methods is generally impossible, as is the use of pure polar solvents or mixtures with high polar solvent contents.

The invention provides a method comprising the following successive steps:

1) synthesis of at least one bifunctional alkenyloxyaryl or alkenylaryloxyaryl type compound with general formula $[R\text{-}CH{=}CH\text{-}(X)\text{-}O]_n\text{-}Ar\text{-}Q$,

where Q is a group which reacts with a hydrogen carried by a heteroatom selected from the group formed by oxygen, nitrogen and sulphur or a precursor of such a group, and where:

- n is in the range 1 to 20;
- R is hydrogen or a linear or branched alkyl group or a linear or branched alkoxy group or a hydroxyl or an aryl group, which may be substituted;
- X is a divalent linear alkyl group containing more than one carbon atom or a divalent branched alkyl group, or an aryl group, which may be substituted with at least one group selected from the group formed by hydrogen, alkyl, alkoxy, hydroxyl or trihalogenoalkyl groups;
- Ar is a divalent aryl or polyaryl group, optionally substituted with at least one hydrogen atom or at least one group selected from the group formed by alkyl, alkoxy, hydroxyl, trihalogenoalkyl, silyl, thiol, amino, aminoalkyl, amide, nitro, nitrosamino, N-amino, aldehyde, acid or ester groups;

2) reacting at least one hydrogen of an alcohol, amine or thiol function of at least one chiral unit of a product, preferably a glycosidic unit of a product selected

from holosides, heteroholisides, oligosides, cyclooligosides, heterooligosides, polyosides, heteropolyosides, enzymes and proteins with at least one group Q of the bifunctional compound of step 1), to synthesise at least one chiral compound.

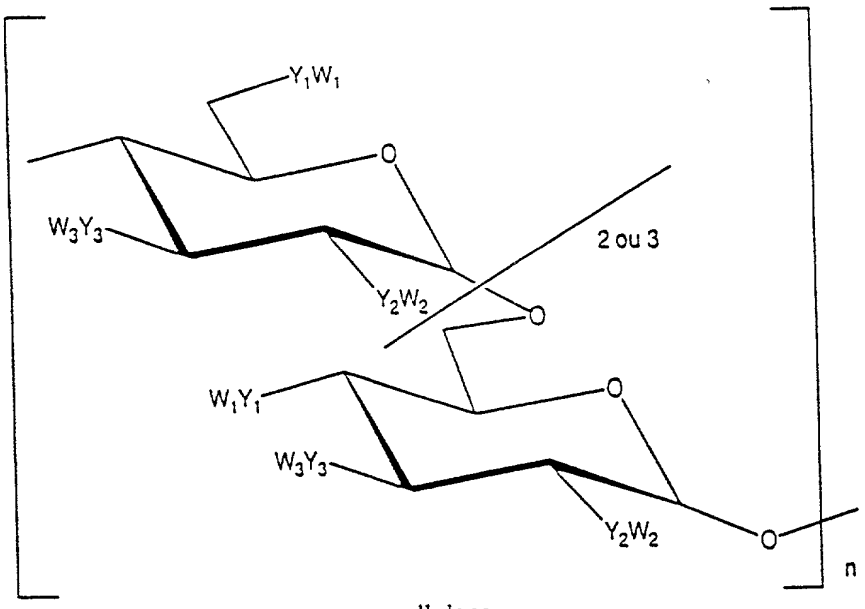
The compound selected from holosides, heteroholisides, oligosides, cyclooligosides, heterooligosides, polyosides, heteropolyosides, enzymes and proteins is generally selected from the following compounds: pullulan, beta-2,1-fructan (inulin), beta-1,4-mannane, cellulose, beta-1,3-glucan curdlan, chitosan, dextran, amylose-cyclodextrins, alpha-1,3-glucan, beta-1,2-glucan, and beta-1,4-xylan, the formula for which are given below.

Group Q is preferably selected from the group formed by the following groups: -N=C=O or a precursor thereof; $-NH_2$, $-CON_3$ or -COCl or a precursor thereof; -COOH, -N=C=S, $-CH_2-Y$, where Y is Cl or Br or I or methylsulphonyloxy or paratoluenesulphonyloxy or 3,5-dimethylphenylsulphonyloxy.

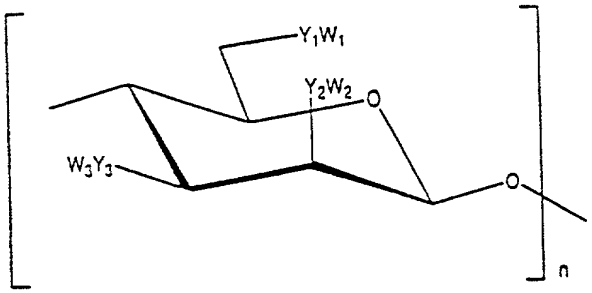
The method of the invention may comprise a supplementary hydrosilylation step, before or after step 2), to transform at least a portion of the alkenyl moieties R-CH=CH- using a silane (R_1, R_2, R_3)Si-H generally in the presence of a metallic complex derived from platinum or rhodium to (R_1, R_2, R_3)-Si-CH(R)-CH_2- moieties, where:

- R_1 is hydrogen or a methoxy or ethoxy group or a halogen or an amino or alkylamino group;
- R_2 and R_3, which may be identical to or different from R_1, are alkoxy, hydroxyl, trihalogenoalkyl, linear or branched alkyl, or aryl groups;
- R is hydrogen or a linear or branched alkyl group or a linear or branched alkoxy group or a hydroxyl group or an aryl group which may be substituted.

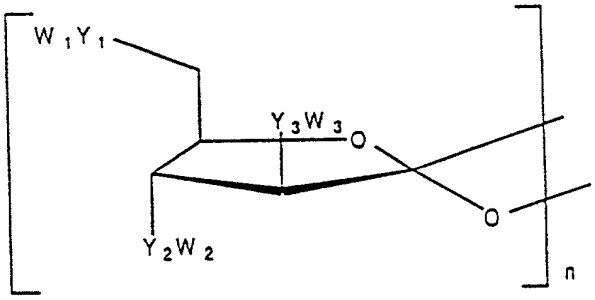
Hydrosilylation generally takes place in a solvent medium in the presence of a suitable catalyst such as platinum.



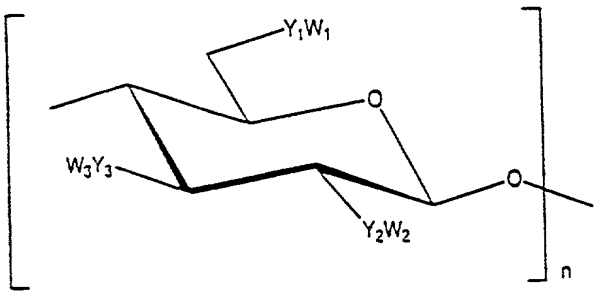
pullulane



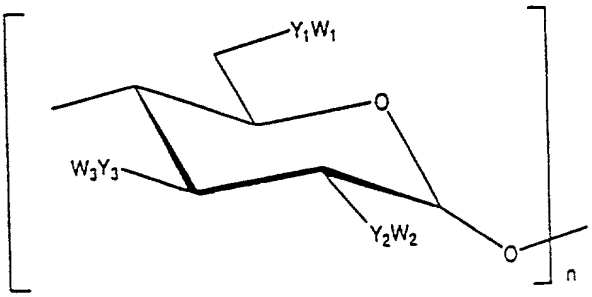
BETA-1,4-MANNANE



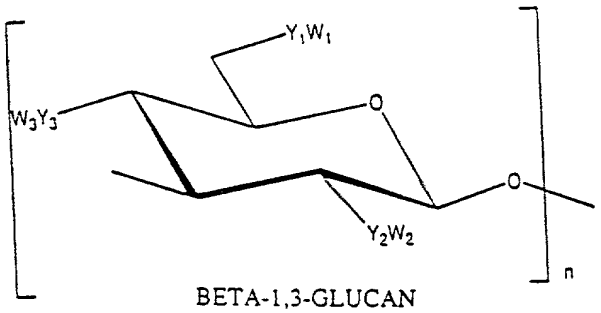
BETA-2,1-FRUCTAN (INULIN)



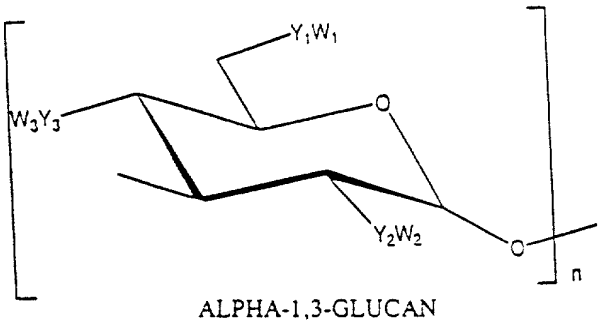
CELLULOSE



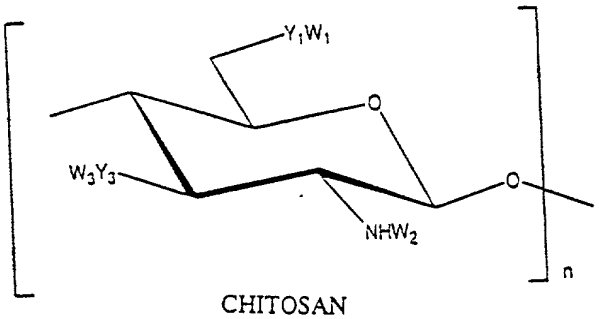
AMYLOSE-CYCLODEXTRIN



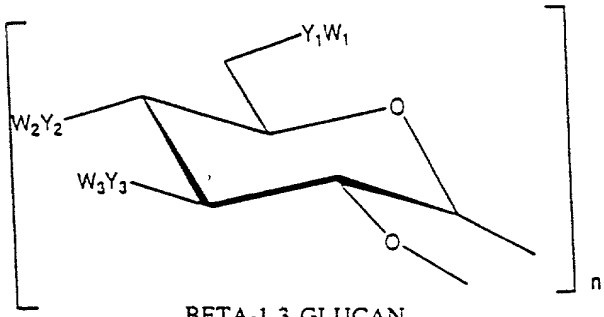
BETA-1,3-GLUCAN
CURDLAN



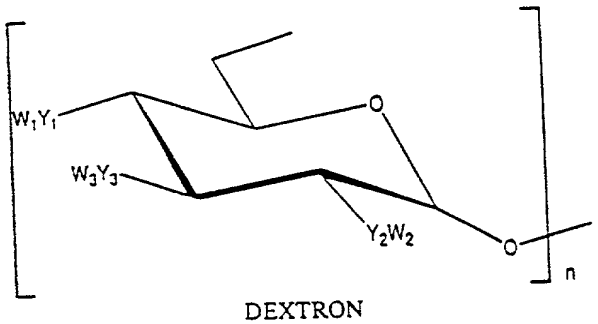
ALPHA-1,3-GLUCAN



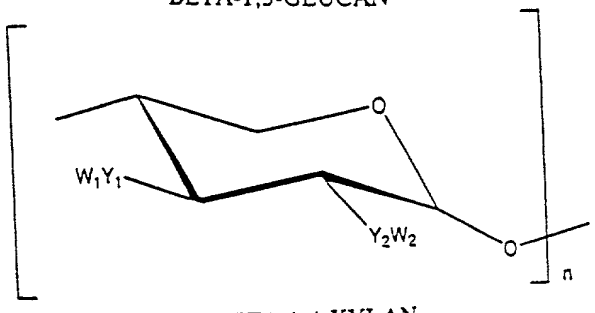
CHITOSAN



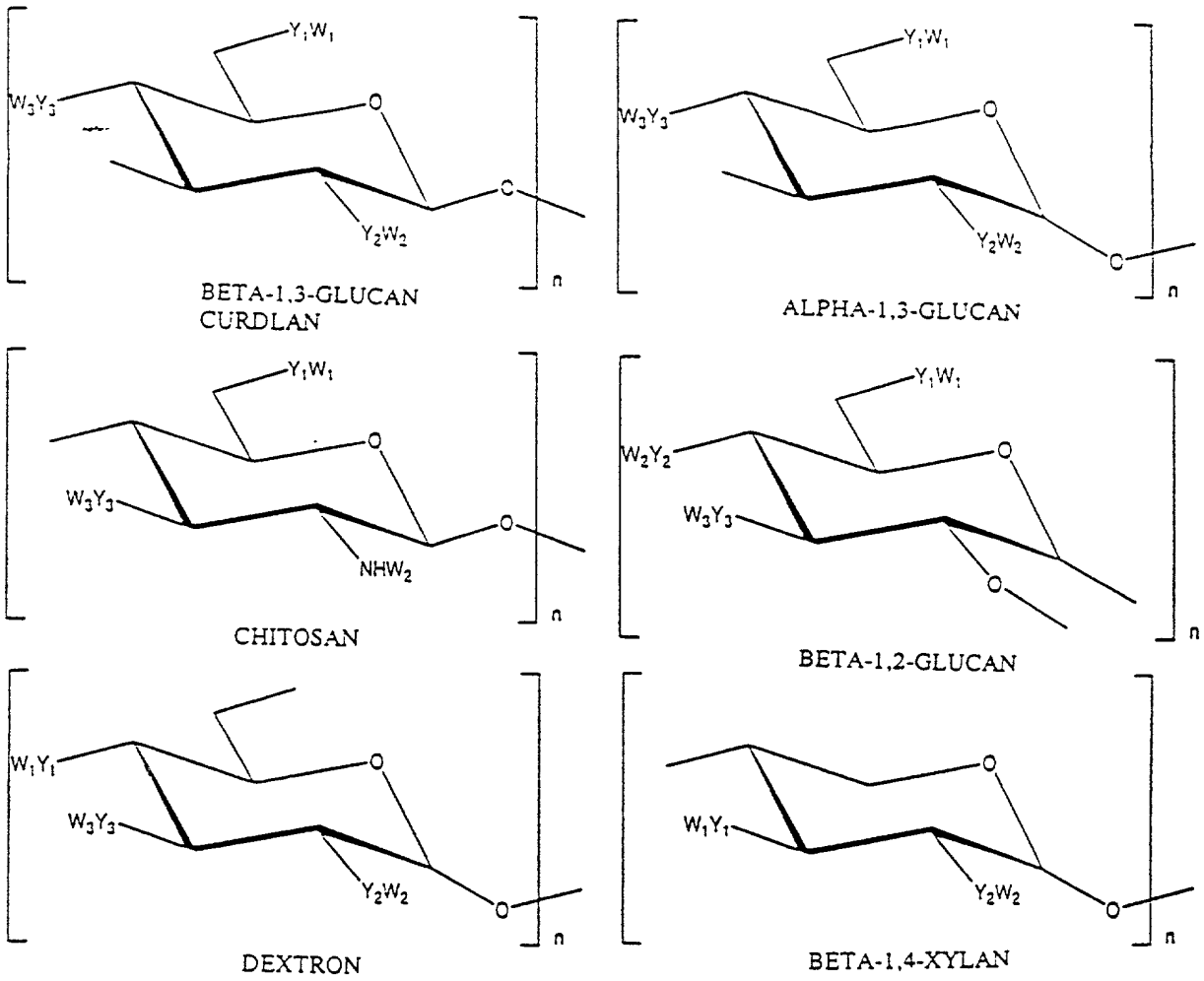
BETA-1,3-GLUCAN



DEXTRON



BETA-1,4-XYLAN



where each Y (Y_1, Y_2 or Y_3) represents a sulphur or oxygen atom or the group NH;

each W (W_1, W_2 or W_3) represents an ethylenic radical with general formula

$[R\text{-}CH{=}CH\text{-}(X)\text{-}O]_n\text{-}Ar\text{-}Z\text{-}$

where Z represents a NH-CO group, or an -NH-CS group, or a CO group, or a CH_2 group;

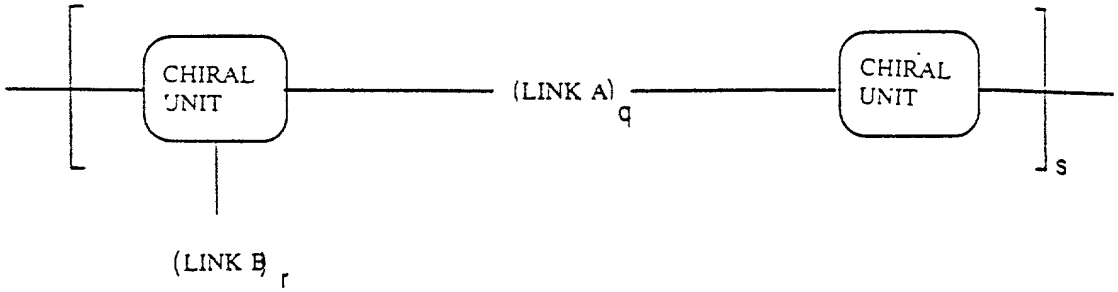
and in which symbols R, X and Ar are defined below;

where n is a whole number in the range 5 to 2000;

and where each glycosidic unit contains at least 0.05 Y-W groups;

groups Y-W may be identical or different.

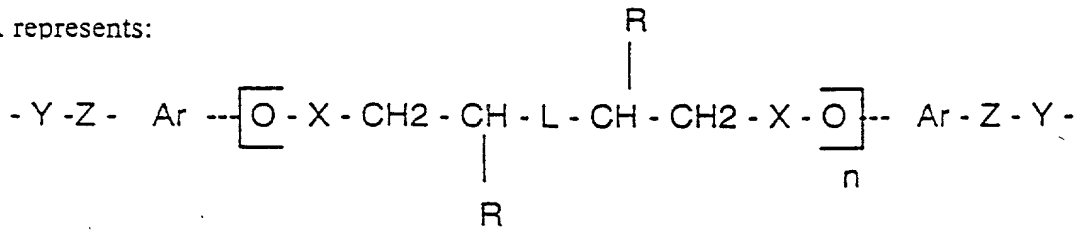
The invention particularly provides a polymerised and cross-linked chiral compound or ester, amide, urea, carbamate, thioester or thiocarbamate derivatives of said polymerised and cross-linked chiral compound, with general formula:



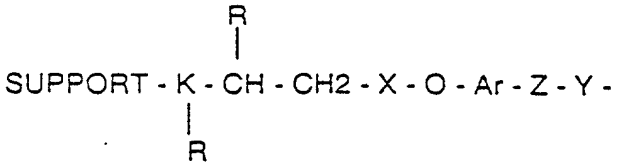
where:

- q is at least 1 and less than 20;
- s is at least 1 and less than 20000;
- if r = 0, the compound is a pure cross-linked chiral polymer, oligomer or monomer;
- if r ≥ 1, the compound is a chiral polymer, oligomer or monomer which is cross-linked in a three-dimensional network and bonded to a cross-linked support.

LINK A represents:



LINK B represents:



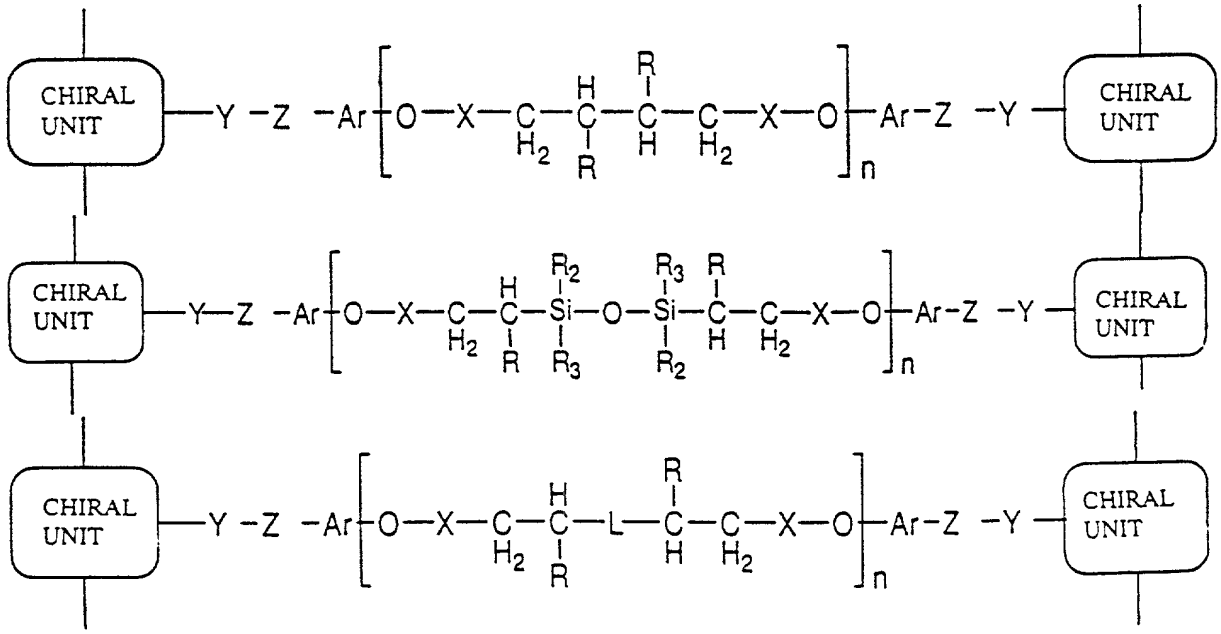
- "chiral unit" represents a monomeric, oligomeric, cyclooligomeric or polymeric chiral compound and optionally comprises a primary or secondary amine

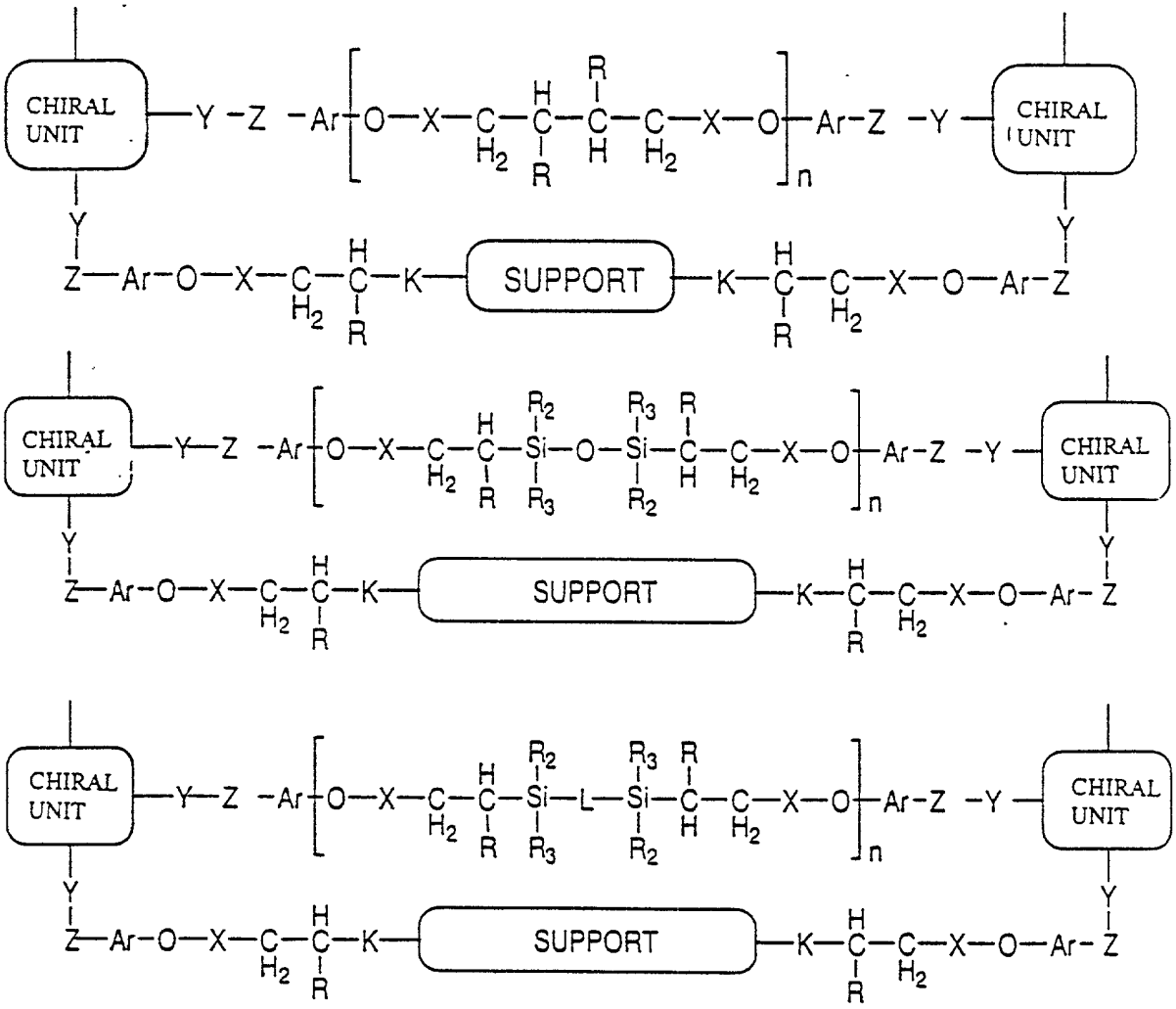
function or a primary, secondary or tertiary hydroxyl function or a sulphhydryl function and in which all or a portion of these functions have optionally been modified to the ester, amide, urea, carbamate, thioester or thiocarbamate;

- Z represents a $-CH_2-$ group or a -CO- group or a -NH-CO- group or a -NH-CS- group;
- Y represents a sulphur or oxygen atom or the amino group;
- n is in the range 1 to 20;
- Ar represents a divalent aryl or polyaryl group;
- X represents a divalent alkyl or aryl group;
- R represents an alkyl group or hydrogen;
- L represents a single bond or a bis-sulphhydryl or silane or an ethylene group which may be substituted or a disiloxane;
- K represents a single bond or a siloxane or a silane;
- "support" represents an organic or mineral support;

functionalised by an alkene or a hydrogenosilane or a sulphhydryl.

Thus the compound or one of its derivatives preferably has one of the following formulae:




CHIRAL UNIT
Y
Z
Ar
O
X
C
H
R
n
SUPPORT
K
CHIRAL UNIT
Y
Z
Ar
O
X
C
H
R
Si
R2
R3
n
SUPPORT
K
CHIRAL UNIT
Y
Z
Ar
O
X
C
H
R
Si
L
R2
R3
n
SUPPORT
K

The method of the invention preferably comprises a supplementary step for treating at least a portion of the chiral compound obtained above to obtain a chiral support. The treatment is generally selected from the group formed by the three treatments described below.

A first treatment for the chiral compound consists of physical deposition of at least a portion of the compound on a support. Such a treatment generally consists of adding a co-solvent to the chiral compound which is dissolved in a polar solvent in the presence of a support, addition being followed by precipitation of the compound on the support, or evaporation of the chiral compound which is dissolved in a polar solvent in the presence of a support.

A second treatment for the chiral compound consists of physical deposition then grafting by covalently bonding at least part of the chiral compound onto a support, the support having been at least partially reacted with at least one group selected from the group formed by alkoxy, halogeno or aminosilane groups to form a derivative, the group also carrying a function of the type -SH, -SiH or -CH=CH-. The second treatment generally comprises adding free alkenyl functions of the portion of the chiral compound to the derivative support followed by in situ cross-linking of the remaining alkenyl functions to constitute a three-dimensional chiral network. The reaction is generally carried out in a solvent with a high boiling point such as a hydrocarbon, to encourage the kinetics. The grafting reaction between at least a portion of the alkenyl functions of the chiral units (preferably glycosidic) of the chiral compound and at least a portion of the -SH, -SiH or -CH=CH- functions of the derivative support generally takes place in an organic solvent in the presence of a suitable catalyst such as platinum salts or peroxides. When the chiral compound has undergone the supplemental hydrosilylation step, grafting is generally carried out on at least a portion of the hydrogen, alkoxy, halogeno or alkylaminosilane type terminal groups.

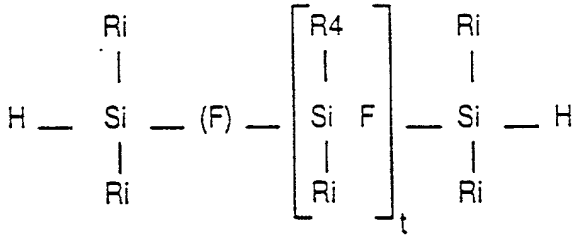
Regarding the first and second treatments, the support is generally selected from the group formed by gel type supports of native or modified silica, oxides of zirconia, magnesium, aluminium, or titanium, glass beads, carbons or any organic polymer.

A third treatment for the chiral compound consists of at least partial polymerisation, generally by cross-linking at least a portion of the chiral compound to obtain polymer beads which essentially constitute a chiral support. One possible manner of carrying out the third treatment generally comprises dissolving the portion of the chiral compound in a suitable solvent then reacting it in a two-phase medium, followed by evaporating the solvent to obtain a polymer in the form of beads or irregular particles, then polymerisation by intra- or inter-molecular cross-linking of at least a portion of the alkenyl moieties of the units, preferably glycosidic, of that portion of the chiral compound, by heating in the presence of a polymerisation initiator such as a peroxide. A further manner of carrying out the third treatment comprises the same steps, with the exception of polymerisation by cross-linking which is obtained by hydrosilylation, using hydrosilanes or hydrosiloxanes, of at least a portion of the alkenyl functions of that portion of the chiral compound on bifunctional dithiol type compounds HS-(...)-SH, dihydrogenosilanes HSi-(...)-SiH, or polyfunctional tetramethyldisiloxane, or 1,3,5,7-tetramethylcyclo-tetrasiloxane, or methylhydrocyclosiloxanes type compounds, or ethanediol type compounds or with sulphur.

Polymerisation by cross-linking is known per se and has been described, for example, in J. Chromatogr. 1992, 594, 283-290. The technique described in this article can be used to prepare the chiral compounds of the invention. In general, the reaction is carried out in a solvent which is inert towards hydrosilylation, such as toluene, 1,4-dioxane, chloroform, tetrahydrofuran (THF)

or xylene, or mixtures of these solvents, at temperatures of 40°C to 140°C. Using a catalyst such as metallic platinum or rhodium complexes accelerates the reaction kinetics.

The hydrosilanes or hydrosiloxanes used to prepare the chiral compounds can be defined by the following general formula:



R^4: is an alkoxy, halogen or alkylamino group;

Ri: is identical to or different from R_1 and is an alkoxy, hydroxyl, aryl, halogen, alkylamino, trihalogenoalkyl, or linear or branched alkyl group;

F: is $(CH_2)_u$ or oxygen;

t: is 0 to 3000;

u: is 0 to 10.

When the chiral compound has undergone a supplemental hydrosilylation step, polymerisation principally occurs by controlled hydrolysis of at least a portion of the terminal hydrogenosilane, alkoxysilane, halogenosilane or N-alkylaminosilane type functions, which mainly results in substantially spherical particles of pure polymer.

The chiral support obtained above by one of the three treatments is preferably used in accordance with the method of the invention in an operation for separating chiral compounds or for preparing enantiomers. The operation is generally selected from the following methods: liquid chromatography, generally preparative or analytical liquid chromatography, comprising the following techniques: low, medium and high pressure (HPLC) liquid chromatography, counter-current chromatography and simulated moving bed chromatography, gas

chromatography, generally analytical or preparative, supercritical chromatography, subcritical chromatography, centrifugal chromatography, electrophoresis, electrochromatography, or any membrane separation process, also asymmetrical synthesis.

The invention also provides a process for synthesising polymers comprising the following successive steps:

1) synthesising at least one bifunctional alkenyloxyaryl or alkenylaryloxyaryl type compound with general formula $[R\text{-}CH{=}CH\text{-}X\text{-}O]_nAr\text{-}Q$,

where Q is a group selected from the group formed by the following groups: -N=C=O or a precursor thereof, $-NH_2$ or $-CON_3$, -COCl or a precursor thereof, -COOH, -N=C=S, $-CH_2Y$, where Y is Cl or Br or I or methylsulphonyloxy or paratoluenesulphonyloxy or 3,5-dimethylphenylsulphonyloxy, and where:

- n is in the range 1 to 20;
- R is hydrogen or a linear or branched alkyl group or a linear or a branched alkoxy group or a hydroxyl or an aryl group, which may be substituted;
- X is a linear or branched alkyl group or an aryl group, which may be substituted with at least one group selected from the group formed by hydrogen, alkyl, alkoxy, hydroxyl and trihalogenoalkyl groups;
- Ar is an aryl or polyaryl group, which may be substituted with at least one hydrogen atom or a group selected from the group formed by alkyl, alkoxy, hydroxyl, trihalogenoalkyl, silyl, thiol, amino, aminoalkyl, amide, nitro, nitrosamino, N-amino, aldehyde,, acid or ester groups;

2) polymerisation by the alkenyl moiety or by the R_1 group of the bifunctional compound of step 1), to synthesise at least one polymer functionalised by a group Q.

The invention also provides any bifunctional alkenyloxyaryl or alkenylaryloxyaryl type compound with general formula $[R\text{-}CH{=}CH\text{-}(X)\text{-}O]_n\text{-}Ar\text{-}Q$,

where Q is a group which is reactive towards a hydrogen carried by a heteroatom selected from the group formed by oxygen, nitrogen and sulphur, or a precursor of such a group, and where:

- n is in the range 1 to 20;
- R is hydrogen or a linear or branched alkyl group or a linear or branched alkoxy group or a hydroxyl or an aryl group, which may be substituted;
- X is an optional divalent linear or branched alkyl group or an aryl group, which may be substituted with at least one group selected from the group formed by hydrogen, alkyl, alkoxy, hydroxyl and trihalogenoalkyl groups;
- Ar is a divalent aryl or polyaryl group, which may be substituted with at least one hydrogen atom or with at least one group selected from the group formed by alkyl, alkoxy, hydroxyl, trihalogenoalkyl, silyl, thiol, amino, aminoalkyl, amide, nitro, nitrosamino, N-amino, aldehyde, acid or ester groups;

excluding the following compounds: 4-allyloxyaniline, 4-allyloxybenzoic acid, its acid chloride, and 4-allyloxyphenylisocyanate. The synthesis and/or use of these compounds is described in the following articles:

- M. A. Apfel, H. Finkelmann, G. M. Janini, R. J. Laub, B. H. Lühmann, A. Price, W. L. Roberts, T. J. Shaw and C. A. Smith, Analytical Chemistry, 1985, 57, 651-658;
- Y. Nambu and T. Endo, Journal of Organic Chemistry, 1993, 58, 1932-1934;
- G. Yi, J. S. Bradhsaw, B. E Rossiter, S. L. Reese, R. Petersson, K. E. Markides and M. L. Lee, Journal of Organic Chemistry, 1993, 58, 2561-2565;
- G. Yi, J. S. Bradhsaw, N. E Rossiter, A. Malik, W. Li, H. Yun, M. L. Lee, Journal of Chromatography A, 673 (1994), 219-230;

- G. Yi, J. S. Bradhsaw, B. E Rossiter, A. Malik, W. Li, H. Yun, M. L. Lee, Journal of Heterocyclic Chemistry, 352, 621 (1995);
- G. Yi, W. Li, J. S. Bradhsaw, A. Malik, M. L. Lee, Journal of Heterocyclic Chemistry, 32, 1715 (1995).

Group Q is preferably selected from the group formed by the following groups: -N=C=O or a precursor thereof, $-NH_2$ or $-CON_3$, -COCl or its precursor, -COOH, -N=C=S, $-CH_2Y$, where Y is Cl or Br or I or methylsulphonyloxy or para-toluenesulphonyloxy or 3,5-dimethylphenylsulphonyloxy.

The invention also provides any chiral compound which can be obtained by a substitution reaction of at least one hydrogen of an alcohol, amine or thiol function of at least one chiral unit of a product, preferably a glycosidic unit of a product selected from holosides, heteroholisides, oligosides, cyclooligosides, heterooligosides, polyosides, heteropolyosides, enzymes and proteins, with at least one group Q of the above bifunctional compound. The invention still further provides any chiral compound which can be obtained by hydrosilylation of the substituted chiral compound to transform at least a portion of the alkenyl moieties R-CH=CH- using a silane (R_1, R_2, R_3)Si-H generally in the presence of a metallic complex derived from platinum or rhodium to (R_1, R_2, R_3)Si-CH(R)-CH_2- moieties, where:

- R_1 is hydrogen or an alkoxy group or a halogen or an amino or alkylamino group;
- R_2 and R_3, which may be identical to or different from R_1, are alkoxy, hydroxyl, trihalogenoalkyl, linear or branched alkyl or aryl groups;
- R is hydrogen or a linear or branched alkyl group or a linear or branched alkoxy group or a hydroxyl group or an aryl group which may be substituted.

The invention yet still further provides any chiral compound which can be obtained by hydrosilylation of a bifunctional compound to transform at least a

portion of the alkenyl moieties R-CH=CH- using a silane (R_1, R_2, R_3)Si-H generally in the presence of a metallic complex derived from platinum or rhodium to (R_1, R_2, R_3)Si-CH(R)-CH_2- moieties, where:

- R_1 is hydrogen or an alkoxy group or a halogen or an amino or alkylamino group;
- R_2 and R_3, which may be identical to or different from R_1, are alkoxy, hydroxyl, trihalogenoalkyl, linear or branched alkyl or aryl groups;
- R is hydrogen or a linear or branched alkyl group or a linear or branched alkoxy group or a hydroxyl group or an aryl group which may be substituted;

then by reacting at least one hydrogen of an alcohol, amine or thiol function of at least one chiral unit of a product, preferably a glycosidic unit of a product selected from holosides, heteroholisides, oligosides, cyclooligosides, heterooligosides, polyosides, heteropolyosides, enzymes and proteins, with at least one group Q of the above bifunctional compound.

The invention also provides any chiral support which can be obtained from the preceding chiral compounds by physical deposition on a support. The invention also provides any chiral support which can be obtained from the above chiral compounds and a support, the support having being derived from at least one group selected from the group formed by alkoxy, halogeno or aminosilane groups also comprising a -SH, -SiH or -CH=CH- type function, by forming covalent chemical bonds with at least a portion of the alkenyl moieties of said chiral compounds followed by in situ cross-linking of the remaining alkenyl functions to constitute a three-dimensional chiral network.

More generally, the invention provides any chiral support comprising at least one of the above chiral compounds and at least one support. The compound is preferably chemically bonded to the support, by at least one covalent chemical bond.

The support is generally selected from the group formed by gel type supports of native or modified silica, oxides of zirconia, magnesium, aluminium or titanium, glass beads, carbons or any organic polymer.

The invention also provides any chiral support which can be obtained from at least one of the above chiral compounds by polymerisation generally by cross-linking at least a portion of the alkenyl moieties of said chiral compound to obtain polymer beads.

More generally, the invention provides any chiral support comprising beads of at least one of the above chiral compounds.

Finally, the invention provides any process for separating chiral compounds or for preparing enantiomers using at least one chiral support as above in an operation selected from the following methods: liquid chromatography, gas chromatography, supercritical chromatography, subcritical chromatography, centrifugal chromatography, electrophoresis, electrochromatography, or any membrane separation process, also asymmetrical synthesis.

The following examples illustrate the invention without in any way limiting its scope.

EXAMPLES

1. Preparation of chromatographic supports in accordance with the invention

a) Preparation of parapent-4-enoxybenzoic acid:

2 g of sodium hydroxide, 15 ml of distilled water, 7.6 g of methyl 4-hydroxybenzoate, 0.16 g of tetrabutylammonium bromide and 5.92 ml of 5-bromopent-1-ene were successively placed in a reactor. Vigorous stirring was maintained overnight at ambient temperature. After adding 30 ml of a 2.5 M sodium hydroxide solution, the reaction medium was heated to 60-80°C for 90 minutes. It was then diluted with 120 ml of distilled water and extracted with two

times 50 ml of diethyl ether. The aqueous phase was acidified with 10 ml of concentrated hydrochloric acid to precipitate the acid. After filtering, washing with distilled water and drying in a dessicator over P_2O_5, the acid was obtained in a yield of 93%.

b) Preparation of the acid chloride of parapent-4-enoxybenzoic acid:

10.3 g of parapent-4-enoxybenzoic acid was suspended in 60 ml of toluene to which 17 ml of thionyl chloride was added. The reaction mixture was heated under reflux for 30 minutes then vacuum evaporated. The oily residue obtained was vacuum distilled (110°C/1 mm of Hg). The yield from this synthesis was 85%.

c) Preparation of parapent-4-enoxybenzoylazide:

A solution of 11.27 g of parapent-4-enoxybenzoyl chloride dissolved in 15 ml of acetone was added dropwise to an aqueous solution of sodium nitride (3.9 g in 22 ml of distilled water) at ambient temperature with vigorous stirring. Following addition, the reaction medium was stirred for one hour then diluted with 50 ml of water. After decanting, the colourless oil obtained was dried over magnesium sulphate. (Yield = 80%).

d) Preparation of parapent-4-enoxyphenylisocyanate

11.6 g of parapent-4-enoxybenzoylazide was dissolved in 80 ml of anhydrous toluene then heated under reflux for 90 min. The solvent was then vacuum evaporated and the residue which had the appearance of a colourless oil was vacuum distilled (100°C/1 mm of Hg). The yield from this synthesis was 94%.

a) Preparation of a tris[1,3,6-(4-allyloxyphenyl)urethane] cellulose (for preparation of a type B support):

2.5 g of microcrystalline cellulose, 75 ml of pyridine and 38 ml of heptane were placed in a reactor. Stirring and heating the reaction mixture dehydrated the cellulose by azeotropic entrainment. 9.31 g of 4-allyloxyphenylisocyanate and 0.05 g of 4-dimethylaminopyridine were added to the mixture and it was heated under reflux for 8 hours. At the end of the reaction, 65 ml of methanol was added and refluxing was continued for 15 minutes. The cellulose derivative was then washed three times with 300 ml of distilled water then 140 ml of methanol.

b) Preparation of a tris[6-(4-allyloxyphenyl)urethane-2,3,6-(3,5-dimethylphenyl)urethane] cellulose (for the preparation of a type A support)

2.5 g of microcrystalline cellulose, 75 ml of pyridine and 38 ml of heptane were placed in a reactor. Stirring and heating the reaction mixture dehydrated the cellulose by azeotropic entrainment. 1.35 g of 4-allyloxyphenylisocyanate, 6.80 g of 3,5-dimethylphenylisocyanate and 0.05 g of 4-dimethylaminopyridine were added to the mixture and it was heated under reflux for 8 hours. At the end of the reaction, 65 ml of methanol was added and refluxing was continued for 15 minutes. The cellulose derivative was then washed three times with 300 ml of distilled water then 140 ml of methanol.

3. Composite obtained between a cellulose derivative and a modified silica (mercaptopropyl silica)

a) Preparation of a mercaptopropyl silica

10 g of Kromasil silica (5 µm, 100- where 1 . = 0.1 nm) suspended in 50 ml of toluene was placed in a reactor. The medium was heated under reflux to dehydrate the silica by azeotropic entrainment. 45 ml of mercaptopropyltrimethoxysilane and 20ml of pyridine were then added. The reaction mixture was stirred and heated at 100°C for two days. After filtering and

washing with methanol and diethylether then vacuum drying at 60°C, a mercaptopropyl silica was obtained with a degree of grafting of 0.85 mmol/g of thiol function.

b) Preparation of composite

b1) For B type support: 0.45 g of tris[2,3,6-(4-allyloxyphenyl)urethane] cellulose was dissolved in 27 ml of tetrahydrofuran, then 3 g of Kromasil mercaptopropyl silica was added. After ultrasound degassing for three minutes, it was evaporated to dryness. The composite formed was filtered, then dried in the open air.

B2) For an A type support: 0.45 g of tris[6-(4-allyloxyphenyl)urethane-2,3,6-(3,5-dimethylphenyl)urethane] cellulose was dissolved in 27 ml of tetrahydrofuran, then 3 g of mercaptopropyl Kromasil silica was added. After ultrasound degassing for three minutes, it was evaporated to dryness. The composite formed was filtered, then dried in the open air.

4-

a) Preparation of a type A chromatographic support:

The composite prepared as above (3-b2) was dissolved in 17 ml of heptane in the presence of a catalytic quantity of benzoyl peroxide. The reaction medium was heated under reflux for 14 hours then filtered and air dried.

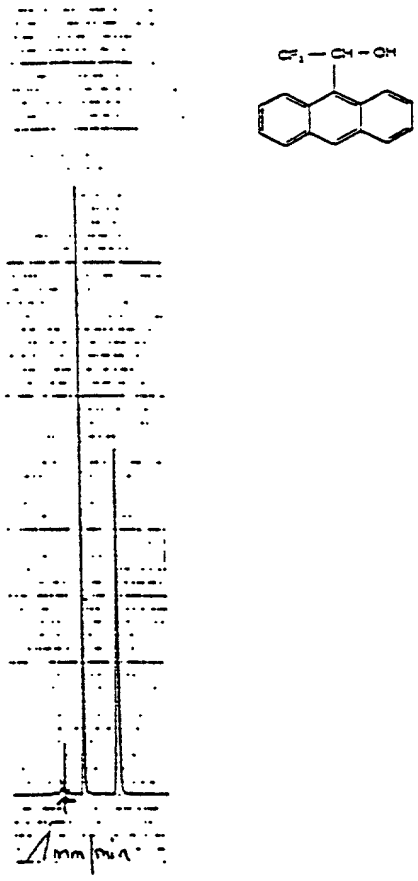
b) Preparation of a type B chromatographic support:

The composite prepared as above (3-b1) was dissolved in 17 ml of heptane in the presence of a catalytic quantity of benzoyl peroxide. The reaction medium was heated under reflux for 14 hours then filtered and air dried.

B- USE OF CHROMATOGRAPHIC SUPPORTS IN ACCORDANCE WITH THE INVENTION

IA - Example of separation on a type A support

Test solute: 2,2,2-trifluoro-1-(9-anthryl)ethanol



*Mobile phase: **100% pure chloroform***

UV detection at 254 nm; O. D. (optical density) = 0.2

Flow rate: 1 ml/min P = 6.2 MPa (600 psi)°

T_0 = 2.95" (non-retained solute transit time measured using 1,3,5,tritert-butylbenzene)

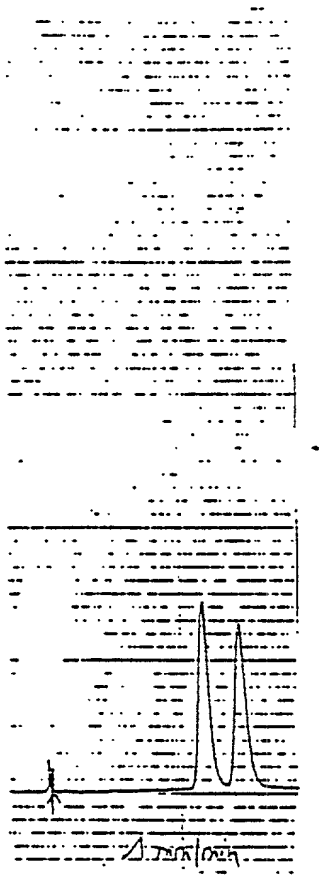
Partition ratios: $k'_1 = 1.03$ $k'_2 = 2.56$

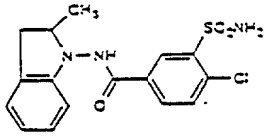
↑: t_0 injection

Relative retention ratio: $\alpha = 2.64$

IB - Example of separation on a type A support

Test solute: indapamide





Mobile phase: ***100% pure chloroform***

UV detection at 254 nm; O. D. = 0.2

Flow rate: 1 ml/min P = 6.2 MPa (600 psi)°

T_0 = 2.95' (non-retained solute transit time measured using 1,3,5,tritert-butylbenzene)

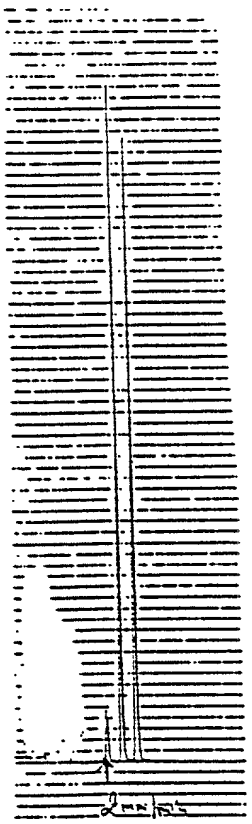
Partition ratios: $k'_1 = 7.47$ $k'_2 = 9.17$

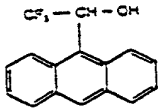
↑: t_0 injection

Relative retention ratio: $\alpha = 1.23$

IC - Example of separation on a type A support

Test solute: 2,2,2-trifluoro-1-(9-anthryl)ethanol





Mobile phase: <u>100% pure dichloromethane</u>

UV detection at 254 nm; O. D. = 0.2

Flow rate: 1 ml/min P = 6.2 MPa (600 psi)°

T_0 = 2.95' (non-retained solute transit time measured using 1,3,5,tritert-butylbenzene)

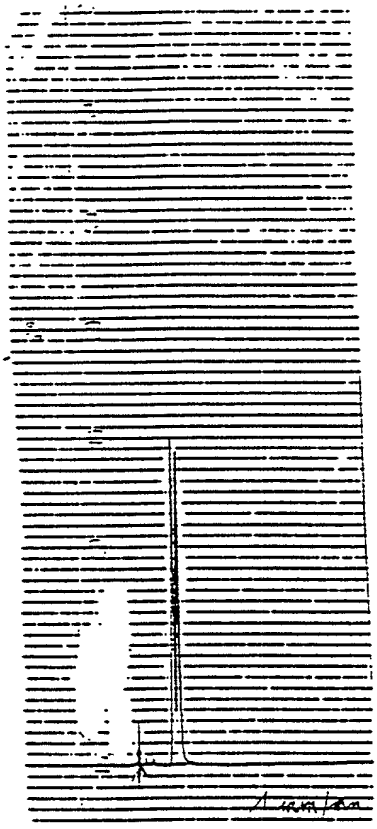
Partition ratios: $k'_1 = 0.56$ $k'_2 = 1.03$

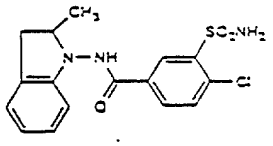
↑: t_0 injection

Relative retention ratio: $\alpha = 1.85$

ID - Example of separation on a type A support

Test solute: indapamide





*Mobile phase: **100% pure dichloromethane***

UV detection at 254 nm; O. D. = 0.2

Flow rate: 1 ml/min P = 6.2 MPa (600 psi)°

T_0 = 2.95' (non-retained solute transit time measured using 1,3,5,tritert-butylbenzene)

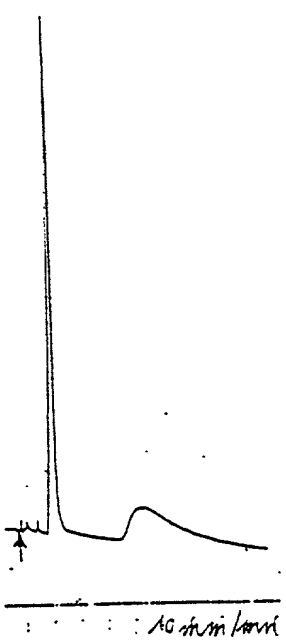
Partition ratios: $k'_1 = 2.13$ $k'_2 = 2.39$

↑: t_0 injection

Relative retention ratio: $\alpha = 1.12$

IE - Example of separation on a type B support

Test solute: oxazepam



Mobile phase: ***70/30/0.1 heptane/isopropanol/diethylamine***

UV detection at 254 nm; O. D. = 0.1

Flow rate: 1 ml/min P = 5.5 MPa (800 psi)°

T_0 = 2.82' (non-retained solute transit time measured using 1,3,5,tritert-butylbenzene)

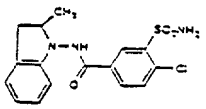
Partition ratios: $k'_1 = 2.69$ $k'_2 = 10.18$

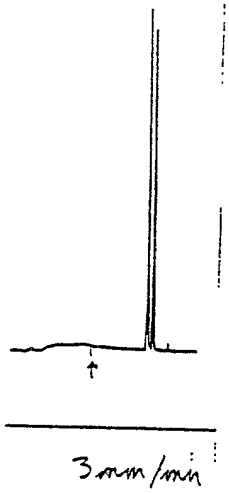
↑: t_0 injection

Relative retention ratio: $\alpha = 3.78$

IIA - Example of separation on a type A support

Test solute: indapamide





Mobile phase: ***reverse mode elution gradient water (100%) to acetonitrile (100%) in 60 minutes***

UV detection at 254 nm; O. D. = 0.5

Flow rate: 1 ml/min

T_0 = 2.80' (non-retained solute transit time measured using 1,3,5,tritert-butylbenzene)

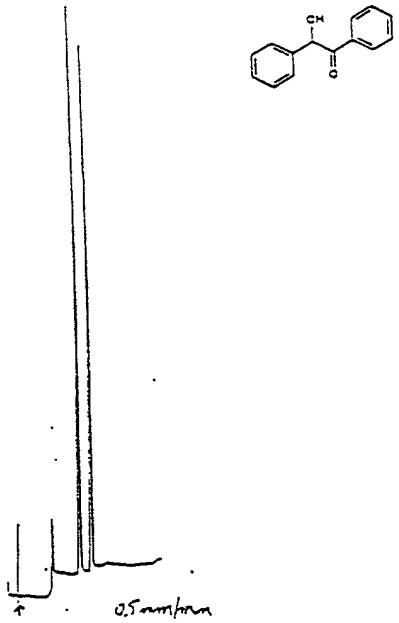
Partition ratios: $k'_1 = 11.03$ $k'_2 = 11.58$

↑: t_0 injection

Relative retention ratio: $\alpha = 1.05$

IIB - Example of separation on a type A support

Test solute: benzoin



Mobile phase: ***normal mode elution gradient***
heptane (100%) to isopropanol (100%) in 60 minutes

UV detection at 254 nm; O. D. = 0.02

Flow rate: 1 ml/min

T_0 = 2.90' (non-retained solute transit time measured using 1,3,5,tritert-butylbenzene)

Partition ratios: $k'_1 = 5.10$ $k'_2 = 6.28$

↑: t_0 injection

Relative retention ratio: $\alpha = 1.23$

III: Example of inversion of order of exit of enantiomers of an active pharmaceutical ingredient on a type A support

Active ingredient (eutomer): 17454

Unwanted enantiomer (distomer): 17455

CONDITIONS 1: 17455 eluted <u>after</u> 17454

Mobile phase: (v = volume)

- hexane 89.4v/methanol 2.4v/isopropanol 8.0v/diethylamine 0.2v 50%
- dichloromethane 10%
- hexane 40%

Retention time of S 17454: 18.29'

Retention time of S 17455: 21.01'

(see diagram below)

CONDITIONS 2: 17455 eluted <u>before</u> 17454

Mobile phase:

- heptane + 2% diethylamine 10%
- dichloromethane 22%
- heptane 66%
- methanol 2%

Retention time of S 17455: 13.86'

Retention time of S 17454: 14.93'

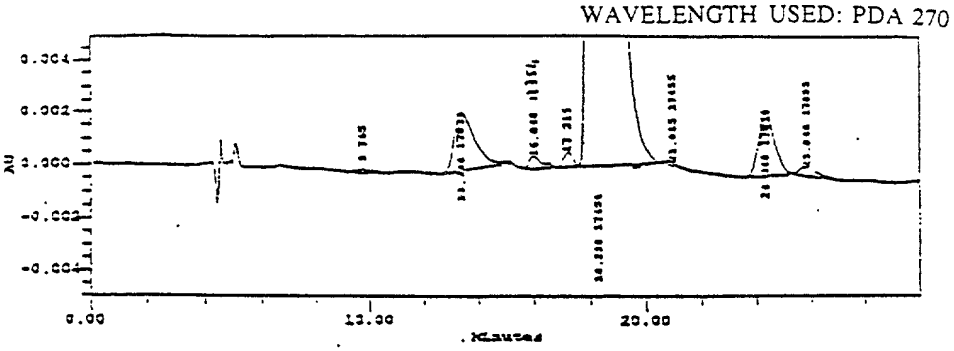
(see diagram below)

Other parameters for conditions 1 and conditions 2 were identical, namely:

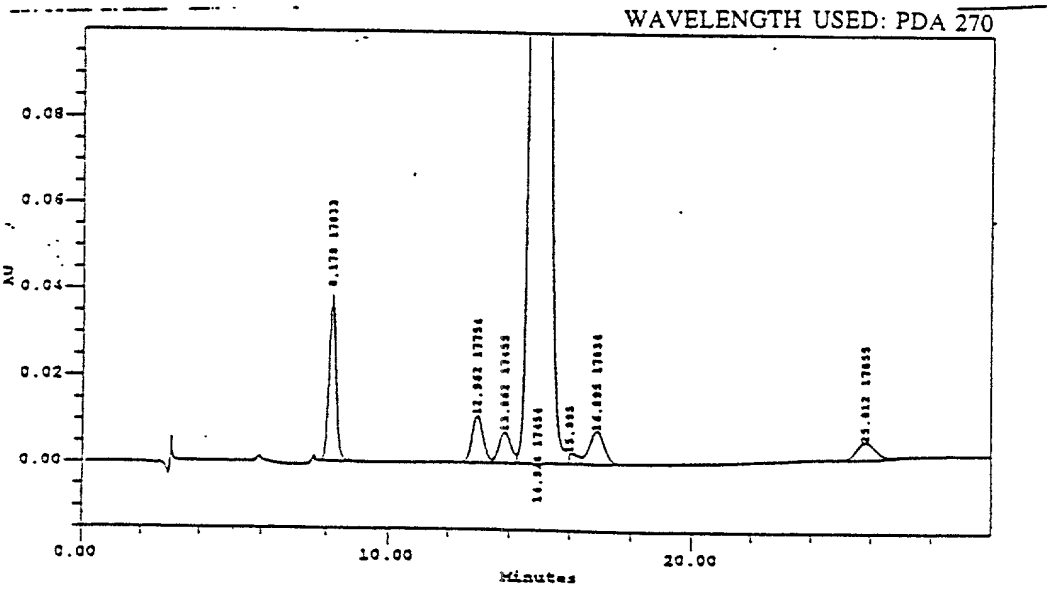
- detection wavelength: 270 nm, UV
- flow rate: 1 ml/min
- 20 µl volume injected, i.e., 20 µg of solute at the concentration used.

III continued

CONDITIONS 1



CONDITIONS 2



The foregoing examples can be repeated with analogous results by substituting the reactants and/or the general or particular conditions described in the invention for those used in the examples.

In the light of the above description, the skilled person can readily determine the essential characteristics of the invention and could make various changes and modifications without departing from the spirit and scope of the invention, to adapt it to various uses and conditions for carrying out the invention.

1. A method comprising the following successive steps:

1) synthesising at least one bifunctional alkenyloxyaryl or alkenylaryloxyaryl type compound with general formula $[R\text{-}CH{=}CH\text{-}(X)\text{-}O]_n\text{-}Ar\text{-}Q$,

where Q is a group which reacts with hydrogen carried by a heteroatom selected from the group formed by oxygen, nitrogen and sulphur or a precursor of such a group, and where:

- n is in the range 1 to 20;
- R is hydrogen or a linear or branched alkyl group or a linear or branched alkoxy group or a hydroxyl or an aryl group, which may be substituted;
- X is a divalent linear alkyl group containing more than one carbon atom or a branched divalent alkyl group, or an aryl group, which may be substituted with at least one group selected from the group formed by hydrogen, alkyl, alkoxy, hydroxyl or trihalogenoalkyl groups;
- Ar is an aryl or polyaryl group, optionally substituted with at least one hydrogen atom or at least one group selected from the group formed by alkyl, alkoxy, hydroxyl, trihalogenoalkyl, silyl, thiol, amino, aminoalkyl, amide, nitro, nitrosamino, N-amino, aldehyde, acid or ester groups;

2) reacting at least one hydrogen of an alcohol, amine or thiol function of at least one chiral unit of a product with at least one group Q of the bifunctional compound of step 1), to synthesise at least one chiral compound.

2. A method according to claim 1, in which group Q is selected from the group formed by the following groups: -N=C=O or a precursor thereof; $-NH_2$, or $-CON_3$, -COC1 or a precursor thereof; -COOH; -N=C=S'; $-CH_2\text{-}Y$,

where Y is C1 or Br or I or methylsulphonyloxy or paratoluenesulphonyloxy or 3,5-dimethylphenylsulphonyloxy.

3. A method according to claim 1 or claim 2, comprising a supplementary hydrosilylation step, before or after step 2), to transform at least a portion of the alkenyl moieties R-CH=CH- using a silane $(R_1, R_2, R_3)Si\text{-}H$ generally in the presence of a metallic complex derived from platinum or rhodium to $(R_1, R_2, R_3)\text{-}Si\text{-}CH(R)\text{-}CH_2\text{-}$ moieties, where:

- R_1 is a hydrogen or a methoxy or ethoxy group or a halogen or an amino or alkylamino

group;

- R_2 and R_3, which may be identical to or different from R_1, are alkoxy, hydroxyl, trihalogenoalkyl, linear or branched alkyl or aryl groups;
- R is hydrogen or a linear branched alkyl group or a linear or branched alkoxy group or a hydroxyl group or an aryl group which may be substituted.

4. A method according to any one of claims 1 to 3, in which the chiral compound is physically deposited on a support to obtain a chiral support.

5. A method according to any one of claims 1 to 3, in which the chiral compound is deposited then grafted onto a support by covalent bonding, the support having been reacted with at least one group selected from the group formed by alkoxy, halogeno or aminosilane groups to form a derivative also carrying a function of the type -SH, -SiH or -CH=CH-, with at least a portion of the alkenyl moieties, to obtain a chiral support.

6. A method according to claim 4 or claim 5, in which the support is selected from the group formed by gel type supports of native or modified silica, oxides of zirconia, magnesium, aluminum or titanium, glass beads, carbons or any organic polymer.

7. A method according to any one of claims 1 to 3, in which the chiral compound is polymerised by cross-linking at least a portion of the alkenyl moieties to obtain polymer beads which essentially constitute a chiral support.

8. A method according to any one of claims 4, 5 or 7, in which the chiral support obtained in the third step is used in an operation for separating chiral compounds or preparing enantiomers.

9. A method according to claim 8, in which said operation is selected from the following methods: liquid chromatography, gas chromatography, supercritical chromatography, subcritical chromatography, centrifugal chromatography, electrophoresis, electrochromatography, or any membrane separation process, also asymmetrical synthesis.

10. A process for synthesising polymers comprising the following successive steps:

1) synthesising at least one bifunctional alkenyloxyaryl or alkenylaryloxyaryl type compound with general formula $[R\text{-}CH{=}CH\text{-}(X)\text{-}O]_n\text{-}Ar\text{-}Q$,

where Q is a group selected from the group formed by the following groups: -N=C=O or a precursor thereof; $-NH_2$ or $-CON_3$; -COC1 or a precursor thereof; -COOH; -N=C=S; $-CH_2Y$, where Y is Cl or Br or I or methylsulphonyloxy or paratoluenesulphonyloxy or 3,5-dimethylphenylsulphonyloxy, and where

- n is in the range 1 to 20;
- R is hydrogen or a linear or branched alkyl group or a linear or branched alkoxy group or a hydroxyl or an aryl group, which may be substituted;
- X is a linear or branched alkyl group or an aryl group, which may be substituted with at least one group selected from the group formed by hydrogen, alkyl, alkoxy, hydroxyl and trihalogenoalkyl groups;
- Ar is an aryl or polyaryl group, optionally substituted with at least one hydrogen atom or with a group selected from the group formed by alkyl, alkoxy, hydroxyl, trihalogenoalkyl, silyl, thiol, amino, aminoalkyl, amide, nitro, nitrosamino, N-amino, aldehyde, acid or ester groups;

2) polymerisation by the alkenyl moiety or by the R_1 group of the bifunctional compound of step 1), to synthesize at least one polymer functionalised by a group Q.

11. A bifunctional alkenyloxyarl or alkenylaryloxyaryl type compound with general formula $[R\text{-}CH{=}CH{=}(X)\text{-}O]_n\text{-}AR\text{-}Q$,

where Q is a group which is reactive towards a hydrogen carried by a heteroatom selected from the group formed by oxygen, nitrogen and sulphur, or a precursor of such a group and where:

- n is in the range 1 to 20;
- R is hydrogen or a linear or branched alkyl group or a linear or branched alkoxy group or a hydroxyl or an aryl group, which may be substituted;
- X is an optional linear alkyl group carrying more than one carbon atom or a branched alkyl group, or an aryl group, which may be substituted with at least one group selected from the group formed by hydrogen, alkyl, alkoxy, hydroxyl and trihalogenoalkyl groups;

- Ar is an aryl or polyaryl group, which may be substituted with at least one hydrogen atom or with at least one group selected from the group formed by alkyl, alkoxy, hydroxyl, trihalogenoalkyl, silyl, thiol, amino, aminoalkyl, amide, nitro, nitrosamino, N-amino, aldehyde, acid or ester groups;

excluding the following compounds: 4-allyloxyaniline, 4-allyloxybenzoic acid, its acid chloride, and 4-allyloxyphenylisocyanate.

12. A compound according to claim 11, in which group Q is selected from the group formed by the following groups: -N=C=O or a precursor thereof; $-NH_2$ or $-CON_3$; -COC1 or its precursor; -COOH; -N=C=S; $-CH_2Y$, where Y is Cl or Br or I or methylsulphonyloxy or para-toluenesulphonyloxy or 3,5-dimethylphenylsulphonyloxy.

13. A chiral compound which can be obtained by reaction of at least one hydrogen of an alcohol, amine or thiol function of at least one chiral unit of a product with at least one group Q of the bifunctional compound according to claim 11 or claim 12.

14. A chiral compound which can be obtained by hydrosilylation of the chiral compound of claim 13 to transform at least a portion of the alkenyl moieties R-CH=CH- using a silane (R_1, R_2, R_3)Si-H generally in the presence of a metallic complex derived from platinum or rhodium to (R_1, R_2, R_3)-Si-CH(R)-CH_2- moieties, where:

- R_1 is a hydrogen or a methoxy or ethoxy group or a halogen or an amino or alkylamino group;
- R_2 and R_3, which may be identical to or different from R_1, are alkoxy, hydroxyl, trihalogenoalkyl, linear or branched alkyl or aryl groups;
- R is hydrogen or a linear branched alkyl group or a linear or branched alkoxy group or a hydroxyl group or an aryl group which may be substituted.

15. A chiral compound which can be obtained by hydrosilylation of the bifunctional chiral compound of claim 11 or claim 12, to transform at least a portion of the alkenyl moieties R-CH=CH- using a silane (R_1, R_2, R_3)-Si-H generally in the presence of a metallic complex derived from a platinum or rhodium to (R_1, R_2, R_3)-Si-CH(R)-CH_2- moieties, where:

- R_1 is a hydrogen or an alkoxy group or a halogen or an amino or alkylamino group;
- R_2 and R_3, which may be identical to or different from R_1, are alkoxy, hydroxyl, trihalogenoalkyl, linear or branched alkyl or aryl groups;

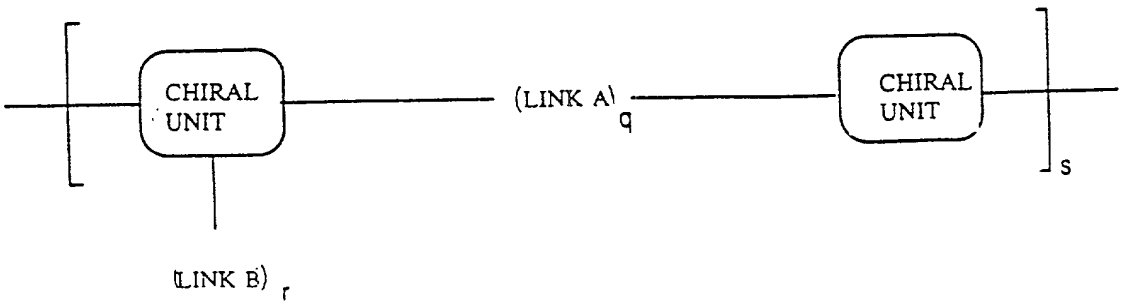
then by reacting at least one hydrogen of an alcohol, amine or thiol function of at least one chiral unit of a product with at least one group Q of the compound of claim 11 or claim 12.

16. A chiral compound which can be obtained by hydrosilylation of an analogous bifunctional compound to the compound according to claim 11 or claim 12, where X represents a methylene group, to transform at least a portion of the alkenyl moieties R-CH=CH- using a silane (R_1, R_2, R_3)Si-H generally in the presence of a metallic complex derived from platinum or rhodium to (R_1, R_2, R_3)Si-CH(R)-CH_2- moieties, where:

- R_1 is a hydrogen or a methoxy or ethoxy group or a halogen or an amino or alkylamino group;
- R_2 and R_3, which may be identical to or different from R_1, are as defined in claim 15.

17. A chiral compound according to any one of claims 1 to 9 or 13 to 16, in which said chiral unit of a product is a glycosidic unit of a product selected from holosides, heteroholisides, oligosides, cyclooligosides, heterooligosides, polyosides, heteropolyosides, enzymes and proteins.

18. A polymerised and cross-linked chiral compound according to any one of claims 13 to 17, or its ester, amide, urea, carbamate, thioester or thiocarbamate derivatives with general formula (I):

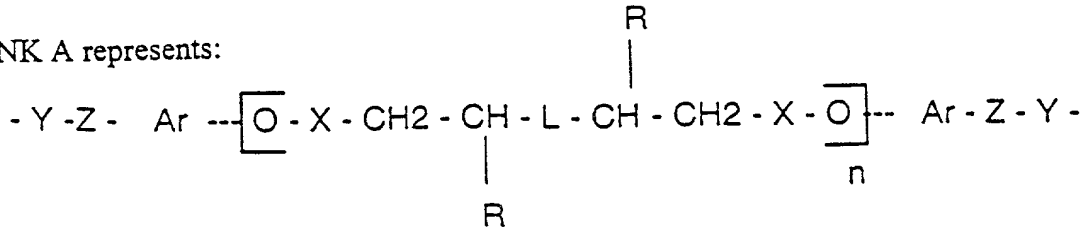


where:

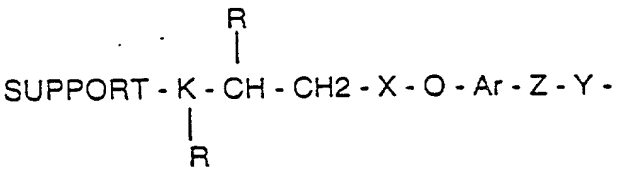
- q is at least 1 and less than 20;
- s is at least 1 and less than 20000;

- if r = 0, the compound is a pure cross-linked chiral polymer, oligomer or monomer;
- if r ≥ 1, the compound is a chiral polymer, oligomer, or monomer which is cross-linked in a three-dimensional network and bonded to a cross-linked support.

LINK A represents:



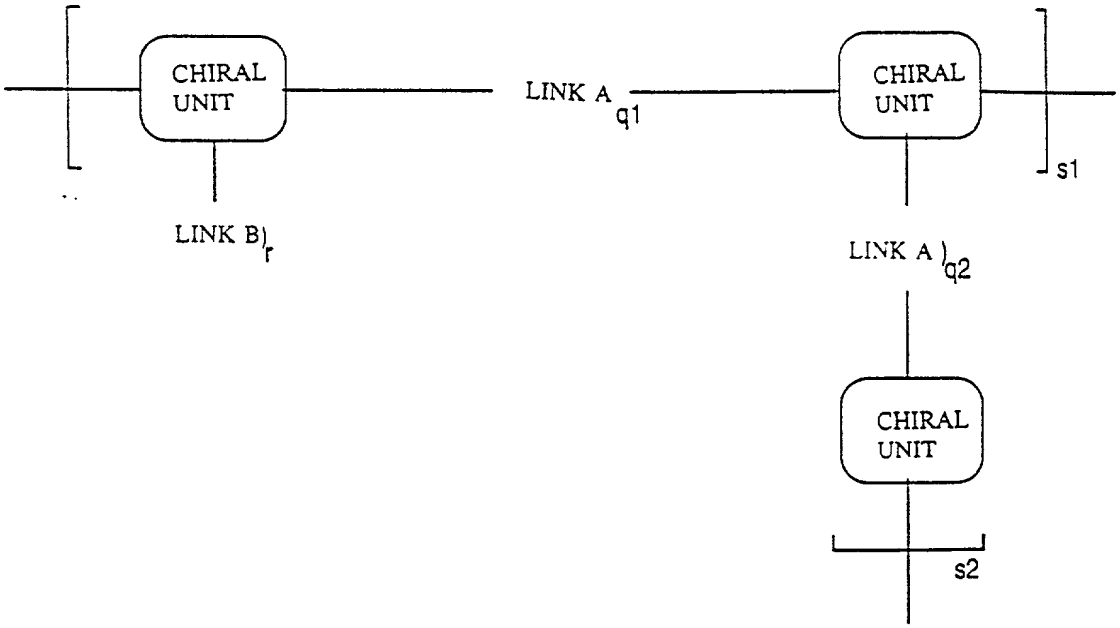
LINK B represents:



- "chiral unit" represents a monomeric, oligomeric, cyclooligomeric or polymeric chiral compound and optionally comprises a primary or second amine function or a primary, secondary or tertiary hydroxyl function or a sulphhydryl function and in which all or a portion of these functions have optionally been modified to the ester, amide, urea, carbamate, thioester or thiocarbamate;
- Z represents a $-CH_2-$ group or a -CO- group or a -NH-CO- group or a -NH-CS- group;
- Y represents a sulphur or oxygen atom or the amino group;
- n is in the range of 1 to 20;
- Ar represents an aryl or polyarl group;
- X represents an alkyl or aryl group;
- R represents an alkyl group or hydrogen;
- L represents a single bond of a bis-sulphhydryl or a silane or an ethylene group which may be substituted or a disiloxane;
- K represents a single bond or a siloxane or a silane;

- "support" represents an organic or mineral support; functionalised by an alkene or a hydrogenosilane or a sulphhydryl.

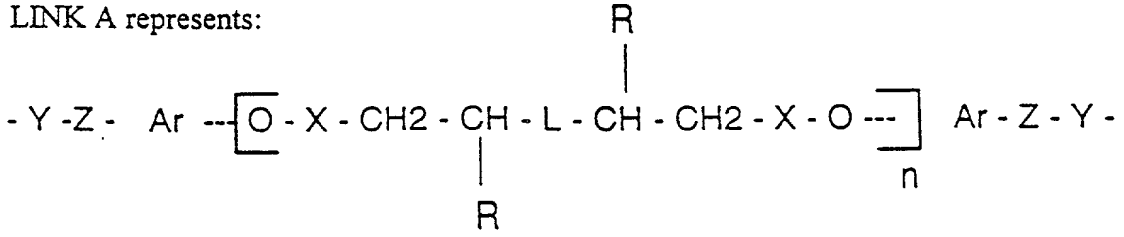
19. A polymerised and cross-linked chiral compound according to any one of claims 13 to 17, or its ester, amide, urea, carbamate, thioester or thiocarbamate derivatives, with general formula:



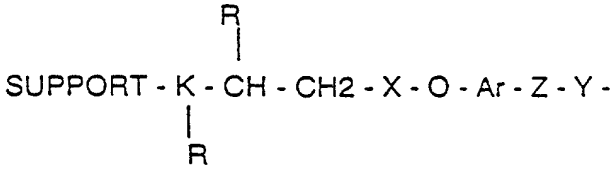
where:

- q_1 and q_2 are each at least 1 and less than 20;
- s_1 and s_2 are each at least 1 and less than 20000;
- if r = 0, the compound is a pure cross-linked chiral polymer, oligomer or monomer;
- if $r \geq 1$, the compound is a chiral polymer, oligomer or monomer which is cross-linked in a three-dimensional network and bonded to a cross-linked support;

LINK A represents:

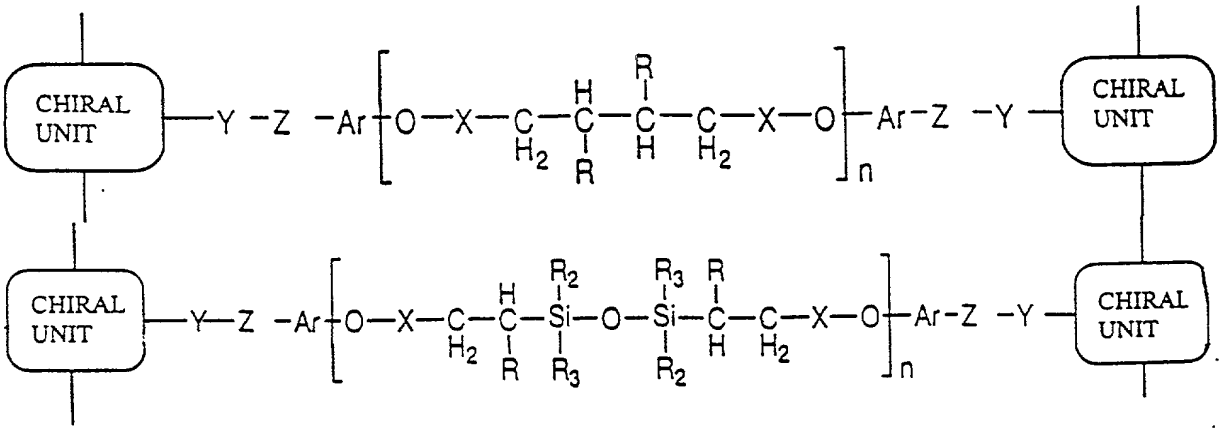


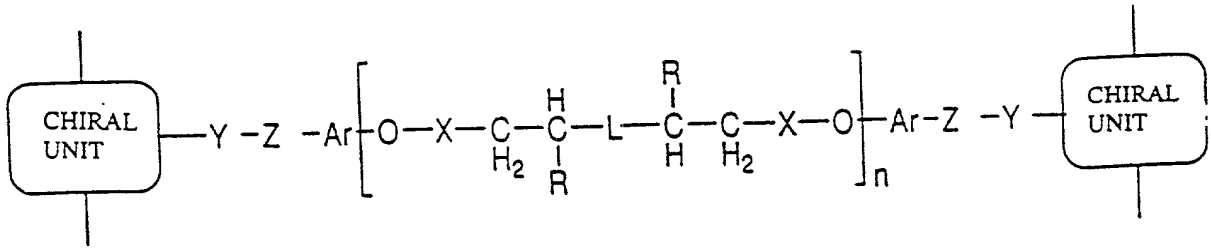
LINK B represents:

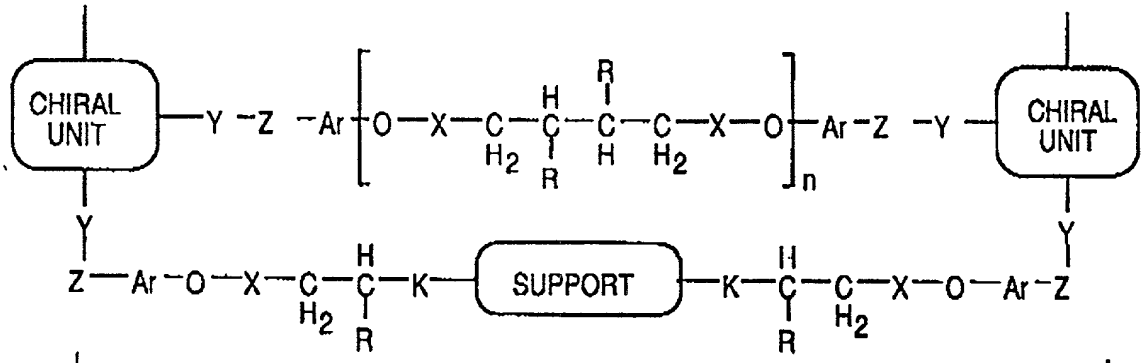


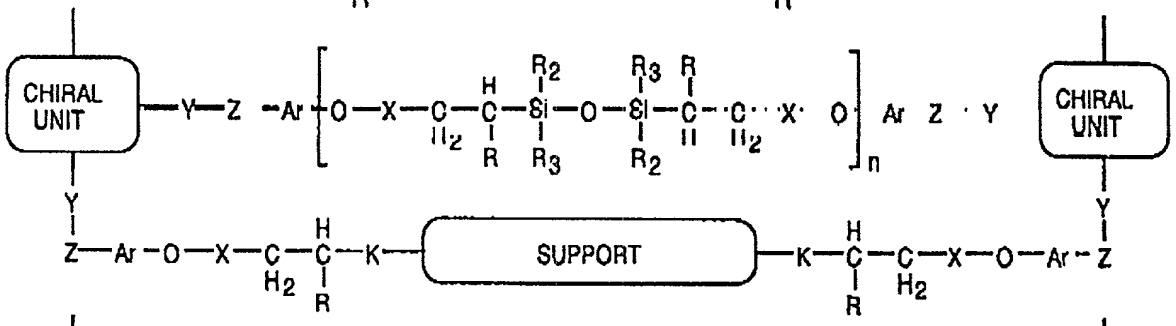
- "chiral unit" represents a monomeric, oligomeric, cyclooligomeric or polymeric chiral compound and optionally comprises a primary or second amine function or a primary, secondar or tertiary hydroxyl function or a sulphhydryl function and in which all or a portion of these functions have optionally been modified to the ester, amide, urea, carbamate, thioester or thiocarbamate;
- Z represents a $-CH_2-$ group or a -CO- group or a -NH-CO- group or a -NH-CS- group;
- Y represents a sulphur or oxygen atom or the amino group;
- n is in the range of 1 to 20;
- Ar represents an aryl or polyarl group;
- X represents an alkyl or aryl group;
- R represents an alkyl group or hydrogen;
- L represents a single bond of a bis-sulphhydryl or a silane or an ethylene group which may be substituted or a disiloxane;
- K represents a single bond or a siloxane or a silane;
- "support" represents an organic or mineral support; functionalised by an alkene or a hydrogenosilane or a sulphhydryl.

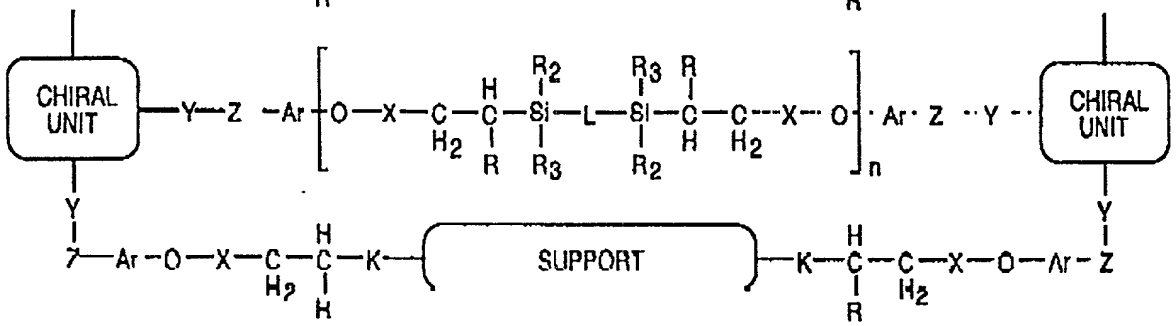
20. A compound according to claim 18, having the following formulae:


CHIRAL UNIT
Y
Z
Ar
O
X
C
H2
H
R
n
CHIRAL UNIT
Y
Z
Ar
O
X
C
H2
H
R
R2
Si
R3
O
Si
R2
R3
R
C
H
H2
X
O
Ar
Z
Y
CHIRAL UNIT


CHIRAL UNIT
Y
Z
Ar
O
X
C
H2
H
R
L
R
C
H
H2
X
O
Ar
Z
Y
CHIRAL UNIT


CHIRAL UNIT
Y
Z
Ar
O
X
C
H2
H
R
n
CHIRAL UNIT
Y
Z
Ar
O
X
C
H2
H
R
K
SUPPORT
K
H
C
R
C
H2
X
O
Ar
Z
Y


CHIRAL UNIT
Y
Z
Ar
O
X
C
H2
H
R
R2
Si
R3
O
Si
R2
R3
R
C
H
H2
X
O
Ar
Z
Y
CHIRAL UNIT
Y
Z
Ar
O
X
C
H2
H
R
K
SUPPORT
K
H
C
R
C
H2
X
O
Ar
Z
Y


CHIRAL UNIT
Y
Z
Ar
O
X
C
H2
H
R
R2
Si
R3
L
Si
R2
R3
R
C
H
H2
X
O
Ar
Z
Y
CHIRAL UNIT
Y
Z
Ar
O
X
C
H2
H
R
K
SUPPORT
K
H
C
R
C
H2
X
O
Ar
Z
Y

21. A chiral support obtainable from a chiral compound according to any one of claims 13 to 19 by physical deposition on a support.

22. A chiral support obtainable from a chiral compound according to any one of claims 13 to 20 and a support, said support having been reacted with at least one group selected from the group formed by alkoxy, halogeno or aminosilane groups to form a derivative, said group also comprising a function of the type -SH, -SiH or -CH=CH-, by forming covalent chemical bonds using at least part of the alkenyl moieties in said chiral compound.

23. A chiral support comprising at least one chiral compound according to any one of claims 13 to 20 and at least one support.

24. A chiral support according to claim 23, in which the chiral compound is chemically bonded to said support, using at least one covalent chemical bond.

25. A chiral support according to any one of claims 21 to 24, in which the support is selected from the group formed by gel type supports of native or modified silica, oxides or zirconia, magnesium, aluminum or titanium, glass beads, carbons or any organic polymer.

26. A chiral support obtainable from a chiral compound according to any one of claims 13 to 20 by polymerisation, generally by cross-linking at least a portion of the alkenyl moieties of said chiral compound to obtain polymer beads.

27. A chiral support comprising beads of a chiral compound according to any one of claims 13 to 20.

28. A process for separating chiral compounds or for preparing enantiomers using a chiral

chromatographic support obtained from any one of claims 21 to 27 in an operation selected from the following methods: liquid chromatography, gas chromatography, supercritical chromatography, subcritical chromatography, centrifugal chromatography, electrophoresis, electrochromatography, or any membrane separation process, also asymmetrical synthesis.

CHIRAL COMPOUNDS, THEIR SYNTHESIS AND USE AS A SUPPORT

ABSTRACT

The invention relates to a method which comprises synthesising bifunctional compounds then chiral compounds from the bifunctional compounds, also to synthesising supports comprising these chiral compounds, and the use of these supports for preparing or separating enantiomers, or for asymmetric synthesis. The invention also relates to bifunctional compounds, their use as a source of functionalised polymers, and to the chiral compounds, also to the use of these chiral compounds in a chiral support in the form of a three-dimensional network or for separating or preparing enantiomers, principally for analytical or preparative chromatography, and in a support for the production of chiral molecules by asymmetric synthesis.

Docket No.

Declaration and Power of Attorney For Patent Application

English Language Declaration

As a below named inventor, I hereby declare that :

My residence, post office address and citizenship are as stated below next to my name,

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled

CHIRAL COMPOUNDS, THEIR SYNTHESIS AND USE AS A SUPPORT

the specification of which

(check one)

☒ is attached hereto.
☐ was filed on ______________ as United States Application No. or PCT international Application Number ______________

and was amended on ______________ (if applicable)

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose to the United States Patent and Trademark Office all information known to me to be material to patentability as defined in Title 37, Code of Federal Regulations, Section 1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, Section 119(a)-(d) or Section 365(b) of any foreign application(s) for patent or inventor's certificate, or Section 365(a) of any PCT International application which designated at least one country other than the United States, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate or PCT International application having a filing date before that of the application on which priority is claimed.

Prior Foreign Application(s)			Priority Not Claimed
97/03.076 (Number)	FRANCE (Country)	14/03/1997 (Day/Month/Year Filed)	☐
(Number)	(Country)	(Day/Month/Year Filed)	☐
(Number)	(Country)	(Day/Month/Year Filed)	☐

I hereby claim the benefit under 35 U.S.C. Section 119(e) of any United States provisional application(s) listed below :

(Application Serial No.)	(Filing Date)
(Application Serial No.)	(Filing Date)
(Application Serial No.)	(Filing Date)

I hereby claim the benefit under 35 U. S. C. Section 120 of any United States application(s), or Section 365(c) of any PCT International application designating the United States, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application in the manner provided by the first paragraph of 35 U.S.C. Section 112. I acknowledge the duty to disclose to the United States Patent and Trademark Office all information known to me to be material to patentability as defined in Title 37, C.F.R., Section 1.56 which became available between the filing date of the prior application and the national or PCT International filing date of this application :

(Application Serial No.)	(Filing Date)	(Status) (patented, pending, abandoned)
(Application Serial No.)	(Filing Date)	(Status) (patented, pending, abandoned)
(Application Serial No.)	(Filing Date)	(Status) (patented, pending, abandoned)

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true ; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

POWER OF ATTORNEY : As a named inventor, I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith. *(list name and registration number)*

I. William Millen (Reg. No. 19,544)
John L. White (Reg. No. 17,746)
Anthony J. Zelano (Reg. No. 27,969)
Alan E.J. Branigan (Reg. No. 20,565)
John R. Moses (Reg. No. 24,983)
Harry B. Shubin (Reg. No. 32,004)
Brion P. Heaney (Reg. No. 32,542)
Richard J. Traverso (Reg. No. 30,595)
Diana Hamlet-King (Reg. No. 33,302)
John A. Sopp (Reg. No. 33,103)
Richard E. Kurtz (Reg. No. 33,936)
Richard M. Lebovitz (Reg. No. 37,067)
John H. Thomas (Reg. No. 33,460)
Luan Cao Do (Reg. No. 38,434)

Send correspondence to : **MILLEN, WHITE, ZELANO & BRANIGAN, P.C.**
Arlington Courthouse Plaza I
2200 Clarendon Blvd., Suite 1400
Arlington, VA 22201

Direct telephone Calls to : *(name and telephone number)*

Full name of sole or first inventor

Raphaël DUVAL

Sole or first inventor's signature Raphaël Duval Date 10/02/98

Residence

60, avenue Amiral Grasset 76330 NOTRE DAME DE GRAVENCHON FRANCE

Citizenship

FRANCE

Post Office Address

60, avenue Amiral Grasset

76330 NOTRE DAME DE GRAVENCHON FRANCE

Full name of second inventor, if any

Hubert LEVEQUE

Second inventor's signature Hubert Lévêque Date 10/02/98

Residence

Résidence d'Alincourt, 11, rue Edmont Pigoreau 76170 LILLEBONNE FRANCE

Citizenship

FRANCE

Post Office Address

Résidence d'Alincourt, 11, rue Edmont Pigoreau

76170 LILLEBONNE FRANCE

